# Medical Policy Bulletin

**Title:**
Ustekinumab for intravenous use
**Policy #:**
MA08.042k

**The Company makes decisions on coverage based on the Centers for Medicare and Medicaid Services (CMS) regulations and guidance, benefit plan documents and contracts, and the member's medical history and condition. If CMS does not have a position addressing a service, the Company makes decisions based on Company Policy Bulletins. Benefits may vary based on contract, and individual member benefits must be verified. The Company determines medical necessity only if the benefit exists and no contract exclusions are applicable. Although the Medicare Advantage Policy Bulletin is consistent with Medicare's regulations and guidance, the Company's payment methodology may differ from Medicare.**

**When services can be administered in various settings, the Company reserves the right to reimburse only those services that are furnished in the most appropriate and cost-effective setting that is appropriate to the member's medical needs and condition. This decision is based on the member's current medical condition and any required monitoring or additional services that may coincide with the delivery of this service.**

**This Policy Bulletin document describes the status of CMS coverage, medical terminology, and/or benefit plan documents and contracts at the time the document was developed. This Policy Bulletin will be reviewed regularly and be updated as Medicare changes their regulations and guidance, scientific and medical literature becomes available, and/or the benefit plan documents and/or contracts are changed.**

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## Policy

**Coverage is subject to the terms, conditions, and limitations of the member's Evidence of Coverage.**

**In the absence of coverage criteria from applicable Medicare statutes, regulations, NCDs, LCDs, CMS manuals, or other Medicare coverage documents, this policy uses internal coverage criteria developed by the Company in consideration of peer-reviewed medical literature, clinical practice guidelines, and/or regulatory status.**

**The Company reserves the right to reimburse only those services that are furnished in the most appropriate and cost-effective setting that is appropriate to the member's medical needs and condition.**

### INITIAL THERAPY WITH USTEKINUMAB PRODUCTS FOR INTRAVENOUS USE

### CROHN DISEASE AND ULCERATIVE COLITIS

Ustekinumab products for intravenous use are considered medically necessary and, therefore, covered for the treatment of individuals with moderately to severely active Crohn disease or moderately to severely active ulcerative colitis when both of the following criteria and the Dosing and Frequency Requirements listed below are met:

- The individual is at least 18 years of age.
- There is documentation of failure, contraindication, or intolerance to a trial of one of the following:
    - Immunomodulators (e.g., azathioprine, 6-mercaptopurine, methotrexate)
    - Corticosteroids (e.g., budesonide [Entocort EC], prednisone, hydrocortisone, methylprednisolone)
    - Biologic therapy (e.g., certolizumab [Cimzia], adalimumab [Humira], infliximab [Remicade]), vedolizumab [Entyvio])

### IMMUNE-CHECKPOINT INHIBITOR–RELATED TOXICITY MANAGEMENT

Ustekinumab products for intravenous use are considered medically necessary and, therefore, covered for the management of the following autoimmune-like toxicities (also known as immune-related adverse events), when

other etiologies have been ruled out and any of the following criteria and the Dosing and Frequency Requirements listed below are met:

- Infliximab- and/or vedolizumab-refractory mild (Grade 1) diarrhea or colitis if persistent or progressive symptoms and positive lactoferrin/calprotectin
- Infliximab- and/or vedolizumab-refractory moderate (Grade 2) or severe (Grade 3-4) diarrhea or colitis

**DOSING AND FREQUENCY OF ADMINISTRATION**

The following dosage and frequency information was taken from the Prescribing Information for this product at the time the policy was being developed:

**CROHN DISEASE AND ULCERATIVE COLITIS, AND IMMUNE-CHECKPOINT INHIBITOR–RELATED TOXICITY MANAGEMENT (DIARRHEA, COLITIS)**

- For initial intravenous infusion:
    - For adults whose weight is up to 55 kg, the recommended dose is 260 mg (two vials)
    - For adults whose weight is more than 55 kg to 85 kg, the recommended dose is 390 mg (three vials)
    - For adults whose weight is more than 85 kg, the recommended dose is 520 mg (four vials)
- Maintenance treatment is administered by subcutaneous formulation

**EXPERIMENTAL/INVESTIGATIONAL**

Use of ustekinumab products in the pediatric population for the treatment of Crohn disease, ulcerative colitis, or immune-checkpoint inhibitor–related toxicities is considered experimental/investigational and, therefore, not covered because the safety and/or effectiveness of this biologic cannot be established by review of the available published peer-reviewed literature.

All other uses of ustekinumab products for intravenous use are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the medical policy on off-label coverage for prescription drugs and biologics.

**DOSING AND FREQUENCY REQUIREMENTS**

The Company reserves the right to modify the Dosing and Frequency Requirements listed in this policy to ensure consistency with the most recently published recommendations for the use of ustekinumab products for intravenous use. Changes to these guidelines are based on a consensus of information obtained from resources such as, but not limited to: the US Food and Drug Administration (FDA); Company-recognized authoritative pharmacology compendia; or published peer-reviewed clinical research. The professional provider must supply supporting documentation (i.e., published peer-reviewed literature) in order to request coverage for an amount of ustekinumab products for intravenous use outside of the Dosing and Frequency Requirements listed in this policy. For a list of Company-recognized pharmacology compendia, view our policy on off-label coverage for prescription drugs and biologics.

Accurate member information is necessary for the Company to approve the requested dose and frequency of this drug. If the member’s dose, frequency, or regimen changes (based on factors such as changes in member weight or incomplete therapeutic response), the provider must submit those changes to the Company for a new approval based on those changes as part of the precertification process. The Company reserves the right to conduct postpayment review and audit procedures for any claims submitted for ustekinumab products for intravenous use.

**REQUIRED DOCUMENTATION**

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include, but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the drug.

When coverage of ustekinumab products for intravenous use is requested outside of the Dosing and Frequency Requirements listed in this policy, the prescribing professional provider must supply documentation (i.e., published peer-reviewed literature) to the Company that supports this request.

**BILLING REQUIREMENTS**

For drugs that have more than one method of administration, application of the JA modifier is required to indicate the route of administration.

- To report the intravenous route of administration, append the following modifier: JA Administered Intravenously

Inclusion of a code in this policy does not imply reimbursement. Eligibility, benefits, limitations, exclusions, utilization management/referral requirements, provider contracts, and Company policies apply.

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## Guidelines

This policy is consistent with Medicare's coverage determination. The Company's payment methodology may differ from Medicare.

Individuals should not be receiving concurrent therapy with any other biologic disease-modifying antirheumatic drug (DMARD) (i.e., anti–tumor necrosis factor agents) while receiving ustekinumab products.

After proper training in subcutaneous injection technique, an individual may self-inject with ustekinumab products if a professional provider determines that it is appropriate. Individuals should be instructed to follow the directions provided in the Medication Guide.

**BENEFIT APPLICATION**

Ustekinumab products for intravenous use is available through either the individual's medical benefit (Part B benefit) or pharmacy benefit (Part D benefit), depending on how the drug is prescribed, dispensed, or administered. This medical policy only addresses instances when ustekinumab products for intravenous use is covered under an individual's medical benefit (Part B benefit), where coverage is based on the medical necessity criteria and Dosing and Frequency Requirements listed in this medical policy. It does not address instances when ustekinumab products for intravenous use is covered under an individual's pharmacy benefit (Part D benefit).

Ustekinumab products may be available under the individual's medical benefits through the Direct Ship Injectables Program.

**US FOOD AND DRUG ADMINISTRATION (FDA) STATUS**

Ustekinumab (Stelara) received FDA approval on September 25, 2009, for the treatment of adults (18 years or older) with moderate-to-severe plaque psoriasis who are candidates for phototherapy or systemic therapy. Supplemental approvals for ustekinumab (Stelara) have since been issued by the FDA for the treatment of psoriatic arthritis, Crohn disease, and ulcerative colitis. The FDA has issued subsequent approvals for biosimilar products.

PEDIATRIC USE

The safety and effectiveness of ustekinumab products for intravenous use in pediatric individuals for the treatment of Crohn disease and ulcerative colitis have not been evaluated.

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## Description

**CROHN DISEASE AND ULCERATIVE COLITIS**

Inflammatory bowel disease (IBD) is a chronic inflammatory disorder of the gastrointestinal tract of unknown etiology. IBD has two major categories: ulcerative colitis (UC) and Crohn disease (CD). The most common symptoms in UC and CD are diarrhea, rectal bleeding, urgency to have bowel movements, abdominal cramps, pain, fever, and weight loss. Even though UC and CD have similar clinical presentations, they differ in the body areas affected. UC primarily causes inflammation of the mucosal lining and is generally limited to the colon and rectum, whereas CD affects the entire digestive system and can produce ulcers that extend deep into the intestinal wall.

The treatment of CD and UC is focused on stopping the inflammation and preventing flare-ups. The type of treatment depends on the type and severity of symptoms. Mild symptoms may respond to an antidiarrheal medicine such as loperamide (e.g., Imodium). Treatment for individuals who may be having mild-to-moderate symptoms include aminosalicylates (and antibiotics for CD), whereas individuals with severe symptoms may be treated with corticosteroids, immunomodulators, or biologics.

**US FOOD AND DRUG ADMINISTRATION (FDA) APPROVAL OF USTEKINUMAB (STELARA)**

Ustekinumab (Stelara) for subcutaneous injection received US Food and Drug Administration (FDA) approval on September 25, 2009, for the treatment of adult individuals (18 years or older) with moderate-to-severe plaque psoriasis and who are candidates for phototherapy or systemic therapy. This indication was later expanded to include pediatric individuals between 6 and 17 years of age with moderate-to-severe plaque psoriasis and who are candidates for phototherapy or systemic therapy. In September 2013, the FDA approved ustekinumab (Stelara) for subcutaneous injection for the treatment of adult individuals (18 years or older) with active psoriatic arthritis, to be used alone or in combination with methotrexate. In September 2016, the FDA approved ustekinumab (Stelara) for intravenous infusion for the treatment of moderately to severely active CD in adult individuals (18 years or older) who have failed or were intolerant to treatment with immunomodulators or corticosteroids but never failed treatment with a tumor necrosis factor (TNF) blocker, or who failed or were intolerant to treatment with one or more TNF blockers. Subsequent maintenance therapy for CD is by subcutaneous injection. In October 2019, the FDA approved ustekinumab (Stelara) for intravenous infusion and subsequent and subcutaneous injection for the treatment of adult individuals (18 years or older) with moderately to severely active ulcerative colitis who have failed or were intolerant to treatment with a biologic, corticosteroids, or immunomodulators.

Ustekinumab (Stelara) is a human IgG1κ monoclonal antibody (a human interleukin-12 and -23 antagonist) that binds with high affinity and specificity to the p40 protein subunit used by both the interleukin (IL)-12 and IL-23 cytokines. IL-12 and IL-23 are naturally occurring cytokines that are involved in inflammatory and immune responses. In in vitro models, ustekinumab (Stelara) was shown to disrupt IL-12 and IL-23 mediated signaling and cytokine cascades.

**PEER-REVIEWED LITERATURE - ADULTS**

SUMMARY FOR CROHN DISEASE
The FDA approval was based on three randomized, double-blind, placebo-controlled clinical studies in adult individuals with moderately to severely active CD (Crohn's Disease Activity Index [CDAI] score of 220 to 450). There were two 8-week intravenous induction studies (CD-1 and CD-2) followed by a 44-week subcutaneous randomized withdrawal maintenance study (CD-3) representing 52 weeks of therapy.

In studies CD-1 and CD-2, 1409 individuals were randomly assigned, of whom 1368 (CD-1, n=741; CD-2, n=627) were included in the final efficacy analysis. Induction of clinical response (defined as a reduction in CDAI score of ≥100 points or CDAI score of <150) at Week 6 and clinical remission (defined as a CDAI score of <150) at Week 8 were evaluated. In both studies, individuals were randomly assigned to receive a single intravenous administration of ustekinumab (Stelara) at either approximately 6 mg/kg, placebo, or 130 mg (a lower dose than recommended).

In Study CD-1, individuals had failed or were intolerant to prior treatment with a tumor necrosis factor (TNF) blocker: 29% of individuals had an inadequate initial response (primary nonresponders), 69% responded but subsequently lost response (secondary nonresponders), and 36% were intolerant to a TNF blocker. Of these individuals, 48% failed or were intolerant to one TNF blocker and 52% had failed two or three prior TNF blockers. At baseline and throughout the study, approximately 46% of the individuals were receiving corticosteroids and 31% of the individuals were receiving immunomodulators (azathioprine, 6-mercaptopurine, methotrexate). The median baseline CDAI score was 319 in the ustekinumab (Stelara) approximately 6 mg/kg group and 313 in the placebo group.

In Study CD-2, individuals had failed or were intolerant to prior treatment with corticosteroids (81% of individuals), at least one immunomodulator (6-mercaptopurine, azathioprine, methotrexate; 68% of individuals), or both (49% of individuals). Additionally, 69% never received a TNF blocker and 31% previously received but had not failed a TNF blocker. At baseline, and throughout the study, approximately 39% of the individuals were receiving corticosteroids and 35% of the individuals were receiving immunomodulators (azathioprine, 6-mercaptopurine, methotrexate). The median baseline CDAI score was 286 in the ustekinumab (Stelara) and 290 in the placebo group. In these induction studies, a greater proportion of individuals treated with ustekinumab (Stelara) achieved clinical response at Week 6 and clinical remission at Week 8 compared to placebo. Clinical response and remission were significant as early as Week 3 in ustekinumab (Stelara)-treated individuals and continued to improve through Week 8.

The maintenance study (CD-3) evaluated 388 individuals who achieved clinical response (≥100 point reduction in CDAI score) at Week 8 of induction with ustekinumab (Stelara) in studies CD-1 or CD-2. Individuals were randomly

assigned to receive a subcutaneous maintenance regimen of either 90 mg ustekinumab (Stelara) every 8 weeks or placebo for 44 weeks. At Week 44, 47% of individuals who received ustekinumab (Stelara) were corticosteroid-free and in clinical remission, compared to 30% of individuals in the placebo group. At Week 0 of Study CD-3, 34 of 56 (61%) ustekinumab (Stelara)-treated individuals who previously failed or were intolerant to TNF blocker therapies were in clinical remission and 23 of 56 (41%) of these individuals were in clinical remission at Week 44. In the placebo arm, 27 of 61 (44%) individuals were in clinical remission at Week 0 while 16 of 61 (26%) of these individuals were in remission at Week 44. At Week 0 of Study CD-3, 46 of 72 (64%) ustekinumab (Stelara)-treated individuals who had previously failed immunomodulator therapy or corticosteroids (but not TNF blockers) were in clinical remission and 45 of 72 (63%) of these individuals were in clinical remission at Week 44. In the placebo arm, 50 of 70 (71%) of these individuals were in clinical remission at Week 0 while 31 of 70 (44%) were in remission at Week 44. In the subset of these individuals who were also naïve to TNF blockers, 34 of 52 (65%) of ustekinumab (Stelara)-treated individuals were in clinical remission at Week 44 as compared to 25 of 51 (49%) in the placebo arm. Individuals who were not in clinical response 8 weeks after ustekinumab (Stelara) induction were not included in the primary efficacy analyses for study CD-3; however, these individuals were eligible to receive a 90-mg subcutaneous injection of ustekinumab (Stelara) upon entry into study CD-3. Of these individuals, 102 of 219 (47%) achieved clinical response 8 weeks later and were followed for the duration of the study.

SUMMARY FOR ULCERATIVE COLITIS
The FDA approval was based on two randomized, double-blind, placebo-controlled clinical studies in 961 adult individuals with moderate to severe UC who had an inadequate response to or failed to tolerate a biologic (i.e., TNF blocker and/or vedolizumab), corticosteroids, or immunomodulators (e.g., 6-MP or AZA therapy). Participants received an intravenous induction dose of ustekinumab (Stelara), either 130 mg (N= 320) or a weight-range-based dose that approximated 6 mg/kg of body weight (N=322), or placebo (N=319), and were reassessed at Week 8. Those who responded were randomly assigned again to receive subcutaneous maintenance injections of 90 mg of ustekinumab (Stelara) either every 12 weeks (N=172) or every 8 weeks (N=176) or placebo (N=175).

The primary end point in the induction trial (Week 8) and the maintenance trial (Week 44) was clinical remission (defined as a total score of ≤2 on the Mayo scale [range, 0–12, with higher scores indicating more severe disease] and no subscore greater than 1 [range, 0–3] on any of the four Mayo scale components). Week 8 results showed those who received ustekinumab (either 130 mg or 6 mg/kg dose) had higher rates of clinical remission compared to placebo (15.6%, 15.5%, vs 5.3%, respectively) ($P$<0.001 for both). Week 44 results showed those who received ustekinumab (either every 12 weeks or every 8 weeks) had higher rates of clinical remission compared to placebo (38.4%, 43.8%, vs 24%, respectively) ($P$=0.002 and $P$<0.001, respectively). The rates of serious adverse events in those who received ustekinumab (Stelara) compared with placebo were similar .

**PEER-REVIEWED LITERATURE - PEDIATRICS**

SUMMARY FOR CROHN DISEASE AND ULCERATIVE COLITIS

As previously mentioned, the first-line therapies for CD or UC may include aminosalicylates, corticosteroids, and immunomodulators. Once an individual has failed or is intolerant to these therapies, a biologic such as infliximab is initiated in the pediatric population. Over time, some individuals lose response to this initial biologic and need another biologic option (Ruemmele et al., 2014; van Rheenen et al., 2020; Turner et al., 2018). Clinical remission for CD or UC may be reported using several scoring systems†, including abbreviated Paediatric Crohn's Disease Activity Index [aPCDAI], partial Mayo Score (PMS), and Harvey-Bradshaw Index (HBI).

The safety and effectiveness of ustekinumab (Stelara) for the treatment of pediatric individuals with CD or UC are still being established. The quality of evidence is low for pediatric individuals with CD, and even lower for those with UC. The evidence is mainly based on case series, retrospective reviews, and small cohort studies with a heterogenous mix of individuals with and without IBD. The limitations of the literature consist of small sample sizes, retrospective designs, heterogeneous population (e.g., dosing not standardized, previous medication exposures). While low quality studies with small data sets, with typically incomplete follow-ups, report clinical remission at a measurable level (40%–60% at 1 year) (Chavannes et al., 2019; Cohen et al., 2020; Dayan et al., 2019), there is a lack of endoscopic data, fecal calprotectin (FC) data, and histologic data to determine the extent of bowel improvement in this subset of individuals. There are no extensive analyses completed in these investigations to demonstrate which attributes an individual possesses to forecast if they will respond to therapy. The limited data in the pediatric population showed a relatively good safety profile (no/few adverse events).

In a systematic review of effectiveness and safety of ustekinumab (Stelara) for pediatric IBD, Fang et al. (2023) reported a reasonable safety profile for ustekinumab (Stelara) (the studies showed no or few adverse events); however, the evidence for efficacy was insufficient due to the nature of the study designs (randomized controlled trial [RCT; n=1], retrospective cohort studies [n=6), case series (n=2)) examined in the review. The

identified RCT was a Phase 1 study with the primary objective of evaluating the pharmacokinetics, and not efficacy, of ustekinumab (Stelara) in pediatric individuals with moderately to severely active CD (Rosh et al., 2021). Researchers only observed a modest increase in clinical remission (22% at week 16) at the lowest dose of ustekinumab (Stelara) without comparison to a proper placebo or active control group (Rosh et al., 2021). These data are not consistent with the clinical remission results (35.9% at week 16) reported for adults given ustekinumab (Stelara) in a real-world study (Casas-Deza et al., 2023). Furthermore, a long-term extension study of the above-mentioned Phase 1 trial resulted in 76.5% (26/34) of individuals discontinuing ustekinumab (Stelara) treatment by week 240 mainly due to lack of efficacy and/or worsening of CD (n=14) in which researchers failed to report on clinical remission success after week 48 (Turner et al., 2024).

Two cohort studies prospectively monitored the efficacy of ustekinumab (Stelara) in pediatric individuals; however, both studies were limited by a small sample size (Dhaliwal et al., 2021; Dolinger et al., 2021). Furthermore, ustekinumab (Stelara) dosing regimens were not standardized and occurred at the discretion of the gastroenterologist, possibly increasing variance and reducing the magnitude of the treatment effects (Dhaliwal et al., 2021). Other limitations included failure to fully comprehend the safety and efficacy of ustekinumab (Stelara) when preceded by various other medications or used as a dual therapy in pediatric individuals (Dolinger et al., 2021). Given the current state of evidence, further clinical trials in pediatric patients are needed to confirm optimal dosing and be confident in the clinical benefit of ustekinumab (Stelara) administration.

Ustekinumab (Stelara) “may be attempted in children and adolescents with active perianal fistulizing disease refractory to anti-TNF agents, but the quality of evidence for a significant effect for this indication in adults is low and data are sparse." The data on the efficacy of ustekinumab (Stelara) after failing anti-TNF agent in pediatric CD are limited (Dayan et al., 2019; Chavannes et al., 2019). The safety profile of ustekinumab (Stelara) in the limited pediatric studies is very good, based on a RCT and clinical experience in the pediatric population with psoriasis (van Rheenen et al., 2020).

There are a few ongoing clinical trials assessing the pharmacokinetics, effectiveness, and/or long-term safety ustekinumab (Stelara) in the pediatric population for the treatment of CD and UC. A large (n=545), observational, retrospective cohort study using real-world evidence of pediatric CD individuals was completed in 2023; however, there are no results available in peer- reviewed literature for this study. There is an ongoing randomized, placebo-controlled, Phase 3 study of the efficacy, safety, and pharmacokinetics of ustekinumab (Stelara) as open-label intravenous induction treatment followed by randomized double-blind subcutaneous ustekinumab (Stelara) maintenance in pediatric individuals with moderately to severely active CD. This study is scheduled for completion in 2025.

While the objective clinical outcome needed to establish effectiveness, namely clinical remission, has been investigated; those data are primarily from studies that lack appropriate controls and were not prospectively conducted.

†Abbreviated Paediatric Crohn's Disease Activity Index [aPCDAI] is a clinical index containing three history items (abdominal pain, number, and consistency of stools and patients functioning) and three physical examinations (weight change, abdominal mass or tenderness, and perirectal disease). The aPCDAI has been found to demonstrate sufficient correlation with the full PCDAI. Scores range from 0 (clinical remission) to 70 (severe, active disease), with the suggested cutoff points being <10 (remission), 10 to 15 (mild disease), 16 to 25 (moderate disease), and >25 (severe disease).

Partial Mayo score [pMS]
The partial Mayo Score (PMS) uses the three noninvasive components of the full Mayo Score (stool frequency, rectal bleeding and Physician's Global Assessment). Each is ranked at a score of 0 to 3; the maximum score is 9.

Harvey-Bradshaw Index (HBI): Five variables recorded on one occasion: General well-being, Abdominal pain, Number liquid stools daily, Abdominal mass, extraintestinal complications.

- Remission: <5
- Mild Disease: 5 to 7
- Moderate Disease: 8 to 16
- Severe Disease: >16

**OFF-LABEL INDICATIONS**

There may be additional indications contained in the Policy section of this document due to evaluation of criteria

highlighted in the Company's off-label policy, and/or review of clinical guidelines issued by leading professional organizations and government entities.

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## Coding

**Inclusion of a code in this table does not imply reimbursement. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.**

**The codes listed below are updated on a regular basis, in accordance with nationally accepted coding guidelines. Therefore, this policy applies to any and all future applicable coding changes, revisions, or updates.**

**In order to ensure optimal reimbursement, all health care services, devices, and pharmaceuticals should be reported using the billing codes and modifiers that most accurately represent the services rendered, unless otherwise directed by the Company.**

**The Coding Table lists any CPT, ICD-10, and HCPCS billing codes related only to the specific policy in which they appear.**

### CPT Procedure Code Number(s)
N/A

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### ICD - 10 Procedure Code Number(s)
N/A

## ICD - 10 Diagnosis Code Number(s)

USTEKINUMAB AND RELATED BIOSIMILARS FOR INTRAVENOUS USE ARE MEDICALLY NECESSARY WHEN REPORTED WITH ANY OF THE FOLLOWING DIAGNOSIS CODES:

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
K51.00 Ulcerative (chronic) pancolitis without complications
K51.011 Ulcerative (chronic) pancolitis with rectal bleeding
K51.012 Ulcerative (chronic) pancolitis with intestinal obstruction
K51.013 Ulcerative (chronic) pancolitis with fistula
K51.014 Ulcerative (chronic) pancolitis with abscess
K51.018 Ulcerative (chronic) pancolitis with other complication
K51.019 Ulcerative (chronic) pancolitis with unspecified complications
K51.20 Ulcerative (chronic) proctitis without complications
K51.211 Ulcerative (chronic) proctitis with rectal bleeding
K51.212 Ulcerative (chronic) proctitis with intestinal obstruction
K51.213 Ulcerative (chronic) proctitis with fistula
K51.214 Ulcerative (chronic) proctitis with abscess
K51.218 Ulcerative (chronic) proctitis with other complication
K51.219 Ulcerative (chronic) proctitis with unspecified complications
K51.30 Ulcerative (chronic) rectosigmoiditis without complications
K51.311 Ulcerative (chronic) rectosigmoiditis with rectal bleeding

K51.312 Ulcerative (chronic) rectosigmoiditis with intestinal obstruction
K51.313 Ulcerative (chronic) rectosigmoiditis with fistula
K51.314 Ulcerative (chronic) rectosigmoiditis with abscess
K51.318 Ulcerative (chronic) rectosigmoiditis with other complication
K51.319 Ulcerative (chronic) rectosigmoiditis with unspecified complications
K51.40 Inflammatory polyps of colon without complications
K51.411 Inflammatory polyps of colon with rectal bleeding
K51.412 Inflammatory polyps of colon with intestinal obstruction
K51.413 Inflammatory polyps of colon with fistula
K51.414 Inflammatory polyps of colon with abscess
K51.418 Inflammatory polyps of colon with other complication
K51.419 Inflammatory polyps of colon with unspecified complications
K51.50 Left sided colitis without complications
K51.511 Left sided colitis with rectal bleeding
K51.512 Left sided colitis with intestinal obstruction
K51.513 Left sided colitis with fistula
K51.514 Left sided colitis with abscess
K51.518 Left sided colitis with other complication
K51.519 Left sided colitis with unspecified complications
K51.80 Other ulcerative colitis without complications
K51.811 Other ulcerative colitis with rectal bleeding
K51.812 Other ulcerative colitis with intestinal obstruction
K51.813 Other ulcerative colitis with fistula
K51.814 Other ulcerative colitis with abscess
K51.818 Other ulcerative colitis with other complication
K51.819 Other ulcerative colitis with unspecified complications
K51.90 Ulcerative colitis, unspecified, without complications
K51.911 Ulcerative colitis, unspecified with rectal bleeding
K51.912 Ulcerative colitis, unspecified with intestinal obstruction
K51.913 Ulcerative colitis, unspecified with fistula
K51.914 Ulcerative colitis, unspecified with abscess
K51.918 Ulcerative colitis, unspecified with other complication
K51.919 Ulcerative colitis, unspecified with unspecified complications
K52.1 Toxic gastroenteritis and colitis

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## HCPCS Level II Code Number(s)

J3358 Ustekinumab, for intravenous injection, 1 mg

Q5098 Injection, ustekinumab-srlf (imuldosa), biosimilar, 1 mg

Q5099 Injection, ustekinumab-stba (steqeyma), biosimilar, 1 mg

Q5100 Injection, ustekinumab-kfce (yesintek), biosimilar, 1 mg

Q5138 Injection, ustekinumab-auub (Wezlana), biosimilar, IV, 1 mg

Q9997 Injection, ustekinumab-ttwe (Pyzchiva), intravenous, 1 mg

Q9998 Injection, ustekinumab-aekn (selarsdi), biosimilar, 1 mg

Q9999 Injection, ustekinumab-aauz (otulfi), biosimilar, 1 mg

**THE FOLLOWING CODES ARE USED TO REPRESENT Starjemza (ustekinumab-hmny):**

C9399 Unclassified drugs or biologics

J3590 Unclassified biologics

## Revenue Code Number(s)

N/A

**THE FOLLOWING MODIFIER IS USED WHEN REPORTING INTRAVENOUS USE**

JA Intravenous administration

## Policy History

**Revisions From MA08.042k:**

| | |
|---|---|
| 09/16/2025 | This version of the policy will become effective 09/16/2025.<br><br>The criterion for Continuation Therapy was removed, since the member will transition from IV initial infusion to SC maintenance (SC is not covered under the Medical Benefit).<br>The management of immunotherapy-related toxicities was updated for infliximab- and/or vedolizumab-refractory mild (Grade 1) symptoms, in alignment with the National Comprehensive Cancer Network (NCCN) compendium. The experimental/investigational position was added for use in the pediatric population in those with Crohn disease, ulcerative colitis, or immune-checkpoint inhibitor–related toxicities.<br><br>The following HCPCS codes have been added to this policy as Medically Necessary:<br>Q5098 Injection, ustekinumab-srlf (imuldosa), biosimilar, 1 mg<br>Q5099 Injection, ustekinumab-stba (steqeyma), biosimilar, 1 mg<br>Q5100 Injection, ustekinumab-kfce (yesintek), biosimilar, 1 mg<br>Q5138 Injection, ustekinumab-auub (Wezlana), biosimilar, IV, 1 mg<br>Q9997 Injection, ustekinumab-ttwe (Pyzchiva), intravenous, 1 mg<br>Q9998 Injection, ustekinumab-aekn (selarsdi), biosimilar, 1 mg<br>Q9999 Injection, ustekinumab-aauz (otulfi), biosimilar, 1 mg<br><br>THE FOLLOWING MODIFIER IS USED WHEN REPORTING INTRAVENOUS USE<br>The JA Modifier (Administered Intravenously) will be appended to:<br>Q5098 Injection, ustekinumab-srlf (imuldosa), biosimilar, 1 mg<br>Q5099 Injection, ustekinumab-stba (steqeyma), biosimilar, 1 mg<br>Q5100 Injection, ustekinumab-kfce (yesintek), biosimilar, 1 mg<br><br>Q9998 Injection, ustekinumab-aekn (selarsdi), biosimilar, 1 mg<br><br>Q9999 Injection, ustekinumab-aauz (otulfi), biosimilar, 1 mg<br><br>THE FOLLOWING CODES ARE USED TO REPRESENT Starjemza (ustekinumab-hmny):<br>C9399 Unclassified drugs or biologics<br>J3590 Unclassified biologics |

**Revisions From MA08.042j:**

| | |
|---|---|
| 03/28/2025 | This policy has been reissued in accordance with the Company's annual review process. |
| 05/07/2024 | This policy has been reissued in accordance with the Company's annual review process. |
| 10/04/2023 | This policy has been reissued in accordance with the Company's annual review process. |
| 07/01/2022 | This version of the policy will become effective 07/01/2022. |

| | |
|---|---|
| | This policy was revised, due to Novitas Solutions, Inc. Article (A53127) For Self-Administered Drug Exclusion List (Revised: 06/06/2022). This policy will only the contain IV formulation of ustekinumab (Stelara); thus the Psoriatic Arthritis and Plaque Psoriasis indications were removed from this policy.<br><br>This policy was also updated to communicate the coverage criteria for the management of immunotherapy-related toxicities (diarrhea, colitits), in alignment with the National Comprehensive Cancer Network (NCCN) compendium.<br><br>*Continuation Therapy section* has been updated with the criteria that the individual has met the coverage criteria for Initial Therapy (in addition to documentation of improvement of symptoms or functions of affected areas.)<br><br>**CODING TABLE:**<br><br>The following HCPCS code has been **deleted** from this policy:<br>J3357 Ustekinumab, for subcutaneous injection, 1 mg<br><br>The following ICD-10 CM code has been **added** to this policy, under the Heading of:<br>**USTEKINUMAB (STELARA) FOR INTRAVENOUS INFUSION**<br>K52.1 Toxic gastroenteritis and colitis<br><br>The following ICD-10 CM codes have been **revised** in this policy, to include a 3rd decimal digit:<br>K50.01**3** Crohn's disease of small intestine with fistula<br>K50.81**9** Crohn's disease of both small and large intestine with unspecified complications<br>K50.91**3** Crohn's disease, unspecified, with fistula<br>K51.31**1** Ulcerative (chronic) rectosigmoiditis with rectal bleeding<br>K51.41**4** Inflammatory polyps of colon with abscess<br><br>The following ICD-10 CM codes have been **deleted** from this policy, under the Heading of: **USTEKINUMAB (STELARA) FOR SUBCUTANEOUS INJECTION IS MEDICALLY NECESSARY WHEN REPORTED WITH THE FOLLOWING DIAGNOSIS CODES:**<br>Crohn's disease: K50.00, K50.011, K50.012, K50.013, K50.014, K50.018, K50.019, K50.10, K50.111, K50.112, K50.113, K50.114, K50.118, K50.119, K50.80, K50.811, K50.812, K50.813, K50.814, K50.818, K50.819, K50.90, K50.911, K50.912, K50.913, K50.914, K50.918, K50.919.<br>Psoraisis, Psoriatic athritis: L40.0, L40.50, L40.51, L40.52, L40.53, L40.59.<br>Ulcerative colitis: K51.00, K51.011, K51.012, K51.013, K51.014, K51.018, K51.019, K51.20, K51.211, K51.212, K51.213, K51.214, K51.218, K51.219, K51.30, K51.31, K51.312, K51.313, K51.314, K51.318, K51.319, K51.40, K51.411, K51.412, K51.413, K51.41, K51.418, K51.419, K51.50, K51.511, K51.512, K51.513, K51.514, K51.518, K51.519, K51.80 , K51.811, K51.812, K51.813, K51.814, K51.818, K51.819, K51.90, K51.911, K51.912, K51.913, K51.914, K51.918, K51.919 |

**Revisions From MA08.042i:**

| | |
|---|---|
| 08/11/2021 | The policy has been reviewed and reissued to communicate the Company's continuing position on ustekinumab (Stelara®). |
| 10/12/2020 | This version of the policy will become effective 10/12/2020.<br><br>This policy was updated to communicate the coverage criteria changes for the expanded FDA approval of ustekinumab (Stelara®) for the treatment of plaque psoriasis to include individuals 6-11 years of age. |

**Revisions From MA08.042h:**

| | |
|---|---|
| 01/06/2020 | This version of the policy will become effective 01/06/2020.<br><br>This policy was updated to communicate the coverage criteria for the new FDA approval of ustekinumab (Stelara®) for the treatment of ulcerative colitis, including dosing and frequency requirements. Prior medications used in Crohn's disease have also been updated. |

**Revisions From MA08.042g:**

| | |
|---|---|
| 09/25/2019 | This policy has been reissued in accordance with the Company's annual review process. |
| 11/21/2018 | This policy has been reissued in accordance with the Company's annual review process. |
| 01/01/2018 | This policy has been identified for the HCPCS code update, effective 01/01/2018.<br><br>The following HCPCS code has been **added** to this policy:<br><br>J3358 Ustekinumab, for intravenous injection, 1 mg<br><br>The following HCPCS code has been **removed** from this policy:<br><br>Q9989 Ustekinumab, for Intravenous Injection, 1 mg |

**Revisions From MA08.042f:**

| | |
|---|---|
| 11/01/2017 | This policy was updated to:<br>• Communicate the new FDA approval for use in adolescents with moderate to severe plaque psoriasis.<br>• Clarify The Company's Dosing and Frequency Requirements for ustekinumab (Stelara®) and the removal of the Risk Evaluation and Mitigation Strategy (REMS) program by the US Food and Drug Administration. |

**Revisions From MA08.042e:**

| | |
|---|---|
| 07/01/2017 | This policy has been identified for the HCPCS code update, effective 07/01/2017.<br><br>The following HCPCS code has been **removed** from this policy:<br>C9487 Ustekinumab, for intravenous injection, 1 mg<br><br>The following NOC code has been **removed** from this policy and is replaced by the following HCPCS code:<br><br>**REMOVED:** J3590 Unclassified biologics<br>**REPLACED WITH:** Q9989 Ustekinumab, for Intravenous Injection, 1 mg |

**Revisions From MA08.042d:**

| | |
|---|---|
| 04/01/2017 | This policy has been identified for the HCPCS code update, effective 04/01/2017.<br>The following HCPCS code has been **added** to this policy:<br>C9487 Ustekinumab, for intravenous injection, 1 mg |

**Revisions From MA08.042c:**

| | |
|---|---|
| 01/01/2017 | This policy has been identified for the HCPCS code update, effective 01/01/2017.<br>The following HCPCS narrative has been **revised** in this policy:<br><br>**FROM:** J3357 Injection, ustekinumab, 1 mg<br>**TO:** J3357 Ustekinumab, for subcutaneous injection, 1 mg |

**Revisions From MA08.042b:**

| | |
|---|---|
| 11/16/2016 | The policy was updated to add coverage for moderately to severely active Crohn's disease.<br><br>The following HCPCS code has been **added** to this policy to represent ustekinumab (Stelara) when administered by intravenous route:<br>• J3590 Unclassified biologics |

| | |
|---|---|
| | Several ICD-10 diagnosis codes have been added to the policy to represent Crohn's disease. |

**Revisions From MA08.042a:**

| | |
|---|---|
| 01/28/2015 | Revised policy number MA08.042a issued as a result of annual policy review. The policy was updated to be consistent with current template wording and format. |

**Revisions From MA08.042:**

| | |
|---|---|
| 01/15/2015 | **New** policy number MA08.042 issued as a result of the development of a separate book of Medicare Advantage policy. Policy's coverage is based on Company medical policy 08.00.82 and was developed with current Medicare Advantage policy Style Guide language and formatting. |

Version Effective Date:
09/16/2025
Version Issued Date:
09/16/2025
Version Reissued Date:
N/A