Entyvio
vedolizumab

Entyvio® (vedolizumab) subcutaneous dosing guide

How to use Entyvio subcutaneous (SC) as maintenance therapy for patients with ulcerative colitis or Crohn's disease

Entyvio is indicated for the treatment of adult patients with moderately to severely active ulcerative colitis (UC) or Crohn's disease (CD) who have had an inadequate response with, lost response to, or were intolerant to either conventional therapy or a tumour necrosis factor-alpha (TNFα) antagonist. Images are not actual size.

C-APROM/IE/ENTY/0300 | August 2023

Takeda

Entyvio. Made for flexibility. Made for simplicity.

Entyvio is available as an IV or SC presentation.[1,2]
Entyvio SC is available as a pre-filled pen.[1]

In an online Takeda survey of UK-based GI nurses who had experience with Entyvio SC Pen (n=32), the Entyvio SC pen was compared with an adalimumab pen, adalimumab syringe and ustekinumab syringe.[3]

In this survey the Entyvio SC pen:[3]

...was most frequently ranked first among nurses for their preference for patient administration

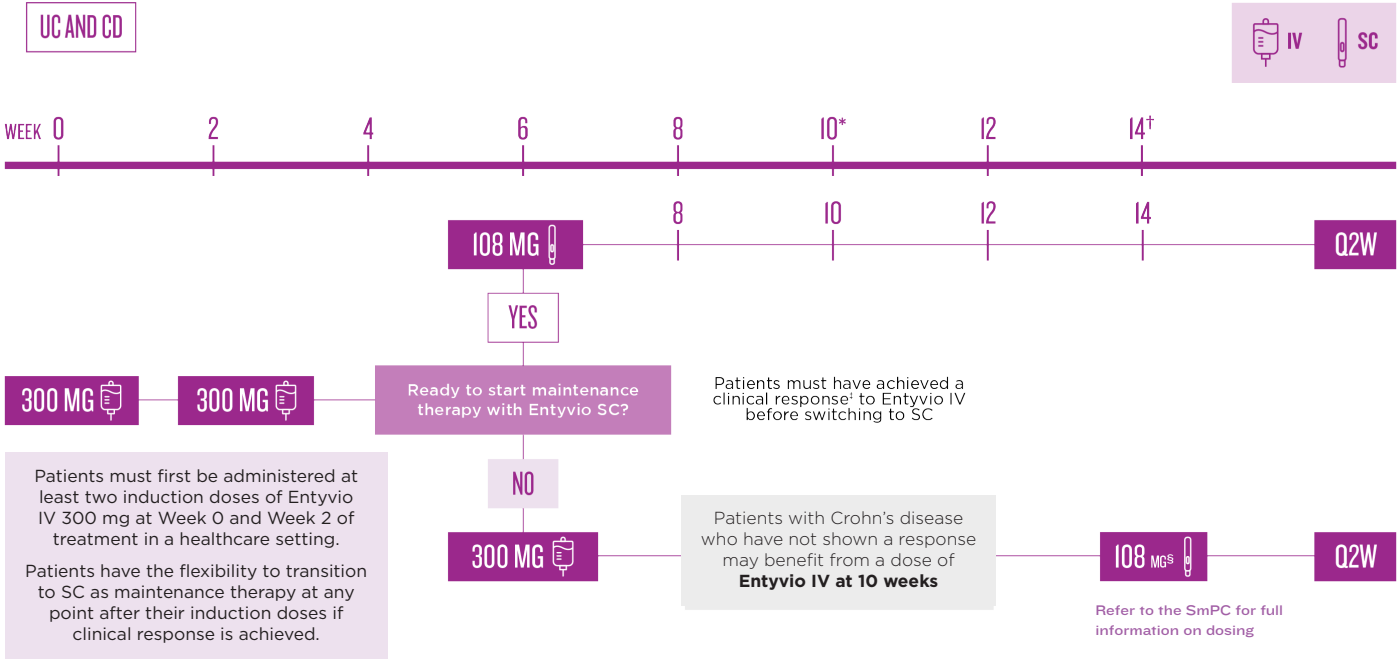
...scored the highest on nurses' preferences for patient comfort

...was rated 'easy' or 'very easy' to demonstrate to patients by 69% of nurses

No reconstitution or calculation is required as each dose is provided in a ready-to-use, single dose device for SC injection.[1]

Entyvio SC dosing schedule for UC and CD

Patients or their caregiver can administer Entyvio SC after training on correct SC injection technique.



*Therapy for patients with UC should be discontinued if no evidence of therapeutic benefit is observed by Week 10.[2] †Therapy for patients with CD should be discontinued if no evidence of therapeutic benefit is observed by Week 14.[2] ‡In UC, clinical response is defined as a reduction in complete Mayo score of ≥3 points and ≥30% from baseline with an accompanying decrease in rectal bleeding subscore of ≥1 point or absolute rectal bleeding subscore of ≤2 points and no individual subscore >1 point.[1] In CD, clinical response is defined as a ≥70-point decrease in the CDAI score from baseline.[1] §In patients with CD who have not shown a response by Week 10 and receive a dose of Entyvio IV at Week 10, Entyvio IV therapy should be continued every 8 weeks from Week 14 in responding patients.[2] These patients with CD responding between Week 10 and 14 can be switched to Entyvio SC Q2W at the next scheduled IV dose, starting at Week 14 or later.[1]

Underpinned by robust data, maintenance with Entyvio SC demonstrates efficacy consistent with the IV presentation for maintenance dosing[2,4]

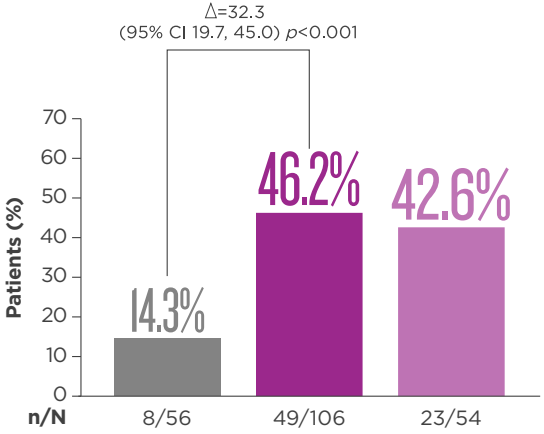
UC

Rates of clinical remission at Week 52 with Entyvio SC in UC were consistent with those with Entyvio IV[4]

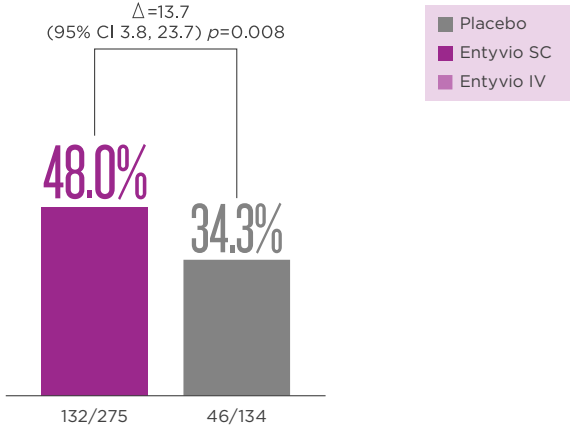
CD

Entyvio SC demonstrated a significantly higher rate of clinical remission at Week 52 vs placebo in CD[5]

VISIBLE 1: Clinical remission* at Week 52[4]



VISIBLE 2: Clinical remission† at Week 52[5]



*Clinical remission: total Mayo score of ≤2 points and no individual subscore >1 point at Week 52 in patients who had achieved a clinical response at Week 6 of intravenous vedolizumab induction treatment.[4] †Clinical remission: defined as CDAI score ≤150 at Week 52.[5] VISIBLE 1 was a Phase 3, randomised, placebo-controlled, double-blind, double-dummy trial. Patients with moderate-to-severe UC received open-label treatment with Entyvio 300 mg IV at Weeks 0 and 2. At Week 6, patients with clinical response were randomly assigned (2:1:1) to maintenance treatment of Entyvio SC (108 mg every 2 weeks), or Entyvio IV 300 mg every 8 weeks, or placebo for up to 52 weeks (n=216).[4] VISIBLE 2 was a Phase 3, randomised, double-blind, placebo-controlled trial. Patients with moderately to severely active CD received open-label treatment with Entyvio 300 mg IV at Weeks 0 and 2. At Week 6, patients with clinical response (n=410) were randomly assigned to maintenance treatment of Entyvio SC (108 mg every 2 weeks) or SC placebo for up to 52 weeks.[5]

Safety findings with Entyvio SC were as expected with the known safety profile of Entyvio IV[2,4,5]

UC

Most frequent AEs (>5% in Entyvio SC or placebo groups) in VISIBLE 1 include:[4]

	VISIBLE 1 Safety analysis set*	
Variable, n (%)	Entyvio SC (n=106)	Placebo (n=56)
Patient with any frequent adverse event	43 (40.6)	32 (57.1)
Disease exacerbation	15 (14.2)	18 (32.1)
Injection-site reactions	11 (10.4)	0 (0.0)
Nasopharyngitis	11 (10.4)	11 (19.6)
Arthralgia	6 (5.7)	1 (1.8)
Upper respiratory tract infection	10 (9.4)	1 (1.8)
Headache	9 (8.5)	6 (10.7)
Anemia	6 (5.7)	2 (3.6)
Sinusitis	1 (0.9)	3 (5.4)

CD

Most frequent AEs (>5% in Entyvio SC or placebo groups) in VISIBLE 2 include:[5]

	VISIBLE 2 Safety analysis set*	
Variable, n (%)	Entyvio SC (n=275)	Placebo (n=134)
Patient with any frequent adverse event†	108 (39.3)	56 (41.8)
Disease exacerbation	42 (15.3)	26 (19.4)
Abdominal pain	21 (7.6)	11 (8.2)
Nasopharyngitis	25 (9.1)	6 (4.5)
Arthralgia	18 (6.5)	9 (6.7)
Upper respiratory tract infection	17 (6.2)	5 (3.7)
Headache	15 (5.5)	5 (3.7)
Nausea	11 (4.0)	7 (5.2)
Vomiting	6 (2.2)	7 (5.2)

For the full list of adverse events please consult the SmPC. *The safety analysis set in VISIBLE 1 and VISIBLE 2 included all patients who were randomised to the maintenance phase and received at least 1 dose of study drug (vedolizumab SC or placebo SC).[4,5] †Defined as an AE with date of onset occurring on or after the first dose of study drug in the induction period through 126 days after the latest dose date or before the first open-label extension dose, whichever occurred earlier.[5]

References & abbreviations

1. Entyvio SC Summary of Product Characteristics. Available at: www.medicines.ie; **2.** Entyvio IV Summary of Product Characteristics. Available at: www.medicines.ie; **3.** Takeda Data on File. EXA/GB/ENTY/0027; **4.** Sandborn WJ, et al. *Gastroenterology* 2020;158:562–572; **5**. Vermeire S, et al. *J Crohns Colitis*. 2022;16:27–38.

AE, adverse event; **CD**, Crohn's disease; **CDAI**, Crohn's Disease Activity Index; **CI**, confidence interval; **GI**, gastrointestinal; **IV**, intravenous; **Q2W**, every two weeks; **SC**, subcutaneous; **SmPC**, Summary of Product Characteristics; **TNF**, tumour necrosis factor; **UC**, ulcerative colitis.

Entyvio® vedolizumab | MADE FOR NOW

ENTYVIO® (vedolizumab) PRESCRIBING INFORMATION FOR REPUBLIC OF IRELAND

Refer to the Summary of Product Characteristics (SmPC) before prescribing.

Presentation: Entyvio intravenous (IV): 300 mg powder for concentrate for solution for infusion. **Entyvio subcutaneous (S/C):** 108 mg solution for injection in pre-filled pen. **Indication: Entyvio IV and Entyvio S/C:** Adult patients with moderately to severely active ulcerative colitis (UC)/Crohn's disease (CD) who have had an inadequate response with, lost response to, or were intolerant to either conventional therapy or a tumour necrosis factor-alpha (TNFα) antagonist. **Entyvio IV only:** Adult patients with moderately to severely active chronic pouchitis, who have undergone proctocolectomy and ileal pouch anal anastomosis for UC, and have had an inadequate response with or lost response to antibiotic therapy. **Dosage and administration:** Treatment should be initiated and supervised by a specialist healthcare professional experienced in diagnosis and treatment of UC, CD or pouchitis. **Entyvio IV:** Patients should be monitored during and after infusion in a setting equipped to manage anaphylaxis. UC: Recommended dose regimen 300 mg administered by IV infusion over 30 minutes at 0, 2, 6 weeks and every 8 weeks thereafter. Discontinue treatment if no evidence of therapeutic benefit by week 10. If patients experience a decrease in response, they may benefit from increased dosage frequency to 300 mg every 4 weeks. Corticosteroids may be reduced/discontinued in patients who respond to treatment with Entyvio. If therapy is interrupted and needs to be restarted, Entyvio dosing every 4 weeks may be considered. CD: Recommended dose regimen is 300 mg administered by IV infusion over 30 minutes at 0, 2, 6 weeks and every 8 weeks thereafter. Patients who have not shown evidence of therapeutic benefit may benefit from a dose at week 10. Continue therapy every 8 weeks from week 14 in responding patients. Therapy should be discontinued if no evidence of therapeutic benefit is observed by week 14. If therapy is interrupted and needs to be restarted, Entyvio dosing every 4 weeks may be considered. Pouchitis: Recommended dose regimen is 300 mg administered by IV infusion at 0, 2 and 6 weeks and then every 8 weeks thereafter. Treatment should be initiated in parallel with standard of care antibiotic (e.g., four-week of ciprofloxacin). Therapy discontinuation should be considered if no evidence of therapeutic benefit is observed by week 14. There are no retreatment data available if therapy is interrupted and needs to be restarted. **Entyvio S/C:** UC and CD: Recommended dose regimen, following at least two IV infusions, is 108mg administered by subcutaneous injection once every 2 weeks. The first S/C dose should be administered in place of the next scheduled IV dose and every 2 weeks thereafter. Insufficient data to determine if patients who experience a decrease in response on maintenance treatment with Entyvio S/C would benefit from an increase in dosing frequency. No data on transition of patients from Entyvio S/C to Entyvio IV during maintenance therapy. Paediatric populations: No data available in children aged 0-17 years. Not recommended. Elderly patients: No dosage adjustment required. Renal or hepatic impairment: Entyvio has not been studied in these populations. No dose recommendation can be given. **Contraindications:** Hypersensitivity to Entyvio or any of the excipients. Active severe infections such as tuberculosis (TB), sepsis, cytomegalovirus, listeriosis and opportunistic infections such as Progressive Multifocal Leukoencephalopathy (PML). **Warnings and precautions: Entyvio IV:** Patients should be observed continuously during infusions for signs/symptoms of hypersensitivity reactions. Patients should continue to be observed for two hours following infusion completion for the first two infusions and one hour for subsequent infusions. Infusion-related reactions (IRR): Hypersensitivity reactions have been reported, the majority were of mild to moderate severity. Discontinue treatment if anaphylaxis or other serious allergic reactions occur and initiate appropriate treatment. In mild to moderate IRR, slow or interrupt infusion. Consideration for pre-treatment with antihistamine, hydrocortisone and/or paracetamol should be given prior to next infusion, for patients with history of mild/moderate IRR to Entyvio. **Entyvio IV and Entyvio S/C:** Infections: Not recommended in patients with active, severe infections until infections are controlled. Consider withholding in patients who develop severe infection while on treatment with Entyvio. Before initiating treatment, patients must be screened for TB. If latent TB is diagnosed, anti-tuberculosis appropriate treatment must be initiated prior to Entyvio treatment. Progressive Multifocal Leukoencephalopathy (PML): John Cunningham (JC) virus infection resulting in PML and death has occurred in patients treated with other integrin receptor antagonists and systemic immunosuppressive agents. A risk of PML cannot be ruled out. Monitor patients for any new or worsening neurological signs/symptoms. Malignancy: Underlying increased risk of malignancy in UC and CD. Immunomodulatory products may increase risk. Prior and concurrent use of biological products: No clinical data available for Entyvio use in patients previously treated with natalizumab or rituximab. Patients previously exposed to natalizumab should wait at least 12 weeks prior to initiating Entyvio therapy. Entyvio not recommended for concomitant use with biologic immunosuppressants as no clinical data available. Live and oral vaccines: Patients may continue to receive non-live vaccines. Patients recommended to be up-to-date with all appropriate immunisations prior to initiating Entyvio. Live vaccines may be administered concurrently only if benefit clearly outweighs risk. **Interactions:** No interaction studies performed. UC and CD: Concomitant administration of corticosteroids, immunomodulators (azathioprine, 6-mercaptopurine, and methotrexate) and aminosalicylates did not have a clinically meaningful effect on Entyvio pharmacokinetics. Pouchitis: Concomitant administration of antibiotics have been observed. The effect on the pharmacokinetics of commonly co-administered medicinal compounds has not been studied. **Fertility, pregnancy and lactation:** There are no data on the effects of vedolizumab on human fertility. Women of childbearing potential should use adequate contraception and continue for at least 18 weeks after last Entyvio treatment. Preferable to avoid use of Entyvio during pregnancy unless benefits clearly outweigh potential risk to both the mother and foetus. Entyvio has been detected in human milk. The effects on breast-fed infants and milk production are unknown. Use of Entyvio in lactating women should consider the benefit of therapy against potential risks to the infant. **Undesirable effects:** No clinically relevant differences in overall safety profile and adverse reactions observed in patients who received Entyvio S/C compared with Entyvio IV except for injection site reactions (with S/C administration). Very Common (≥1/10): nasopharyngitis, headache, arthralgia. Common (≥1/100, <1/10): injection site reactions (Entyvio S/C only), pneumonia, Clostridium difficile infection, bronchitis, gastroenteritis, upper respiratory tract infection, influenza, sinusitis, pharyngitis, herpes zoster, paraesthesia, hypertension, oropharyngeal pain, nasal congestion, cough, anal abscess, anal fissure, nausea, dyspepsia, constipation, abdominal distension, flatulence, haemorrhoids, rectal haemorrhage*, rash, pruritus, eczema, erythema, night sweats, acne, muscle spasm, back pain, muscular weakness, fatigue, pain in extremity, pyrexia, infusion related reaction (asthenia* and chest discomfort*), infusion site reaction (including: infusion site pain and infusion site irritation). *Reported in the EARNEST pouchitis study. Uncommon (≥ 1/1,000 to < 1/100): respiratory tract infection, blurred vision. Very rare (< 1/10,000): anaphylactic reaction, anaphylactic shock. Not known: interstitial lung disease. **Refer to the SmPC for details on full side effect profile and interactions. Legal Classification:** POM. **Marketing authorisation (MA): Entyvio IV:** EU/1/14/923/001. **Entyvio S/C:** EU/1/14/923/005. **Name and Address of MA holder:** Takeda Pharma A/S, Delta Park 45, 2665 Vallensbaek Strand, Denmark. Additional information is available on request at: medinfoemea@takeda.com. **PI Approval Code:** pi-02511. **Date of revision:** July 2023.

Adverse Events should be reported to the Pharmacovigilance Unit at the Health Products Regulatory Authority. Reporting forms and information can be found at: www.hpra.ie. Adverse events should also be reported to Takeda at: AE.GBR-IRL@takeda.com.