Entyvio® (vedolizumab)
Instructions for reconstitution, infusion and monitoring[1]

Entyvio is indicated for the treatment of adult patients with moderately to severely active Ulcerative Colitis or Crohn's Disease who have had an inadequate response with, lost response to, or were intolerant to either conventional therapy or a tumour necrosis factor-alpha (TNFa) antagonist.

1

- Use aseptic technique when preparing Entyvio solution for intravenous infusion
- Remove vial from refrigeration and allow it to equilibrate to room temperature
- Entyvio should be at room temperature (20°C–25°C) when reconstituted
- Remove flip-off cap from the vial and wipe with alcohol swab

2

- Reconstitute Entyvio with 4.8ml of sterile water for injection, using a syringe with a 21–25 gauge needle
- Insert the syringe needle into the vial through the centre of the stopper and direct the stream of sterile water towards the wall of the vial to avoid excessive foaming

3

- Gently swirl the vial for at least 15 seconds
- Do not vigorously shake or invert

4

- Allow the vial sit for up to 20 minutes to allow for reconstitution and for any foam to settle; the vial can be swirled and inspected for dissolution during this time
- If not fully dissolved after 20 minutes, allow another 10 minutes for dissolution

5

- Visually inspect the reconstituted solution for particulate matter and discoloration prior to administration
- Solution should be clear or opalescent, colourless to light yellow and free of visible particulates
- Reconstituted solution with uncharacteristic colour or containing particulates must not be administered

6

- Prior to withdrawing reconstituted solution from vial, gently invert the vial three times to ensure it is adequately mixed

7

- Withdraw 5ml (300mg) of reconstituted Entyvio using a syringe with a 21–25 gauge needle

8

- Add the 5ml (300mg) of reconstituted Entyvio to 250ml of sterile 0.9% sodium chloride solution, and gently mix the infusion bag
- Do not add other medicinal products to the prepared infusion solution or intravenous infusion set

9

- Administer the infusion solution over 30 minutes
- Patients should be monitored during and after infusion and for two hours after their first two infusions for signs and symptoms of acute hypersensitivity reactions
- Monitoring can be reduced to one hour for subsequent infusions
- Each Entyvio vial is for single-use only
- Any unused product or waste material should be disposed of in accordance with local requirements

Starting materials

Materials	Quantity
Glass vial of Entyvio® 300mg	**1**
Sterile water for reconstitution	**4.8ml**
Sterile 0.9% NaCl-solution	**1 infusion bag of 250ml**
21-25 gauge needles	**2**
5ml syringes	**2**

Entyvio does not contain preservatives. Once reconstituted, the infusion solution should be used as soon as possible. If necessary, the infusion solution may be stored for up to 24 hours: this 24 hour hold may include up to 12 hours at 20–25°C; any additional hold time must be at 2–8°C. Do not freeze. Do not store any unused portion of the infusion solution for reuse[1].

Entyvio® ▼ (vedolizumab) This medicinal product is subject to additional monitoring. **PRESCRIBING INFORMATION**

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

Presentation: 300mg powder for concentrate for solution for infusion. **Indication:** *Ulcerative colitis (UC):* Adult patients with moderately to severely active ulcerative colitis 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. *Crohn's disease (CD):* Adult patients with moderately to severely active Crohn's disease 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. **Dosage & Administration:** Treatment should be initiated and supervised by a specialist healthcare professional experienced in the diagnosis and treatment of ulcerative colitis or Crohn's disease. Patients should be monitored during and after infusion. *Ulcerative colitis:* Recommended dose regimen is 300mg administered by intravenous infusion over 30 minutes at 0, 2 and 6 weeks and then every 8 weeks thereafter. Reconsider treatment if no evidence of therapeutic benefit at week 10. If patients experience a decrease in their response, they may benefit from an increased dosage frequency of 300mg 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. *Crohn's disease:* Recommended dose regimen is 300mg administered by intravenous infusion over 30 minutes at 0, 2 and 6 weeks and then 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 at week 14. If therapy is interrupted and needs to be restarted, Entyvio dosing every 4 weeks may be considered. *Paediatric populations:* No data is available on the safety and efficacy of Entyvio in children aged 0-17 years. *Elderly patients:* No dosage adjustment required. *Renal or hepatic impairment:* Entyvio has not been studied in these populations and no dose recommendation can be given. **Contraindications:** Hypersensitivity to Entyvio or any of the excipients. Active infections such as tuberculosis (TB), sepsis, cytomegalovirus, listeriosis and opportunistic infections such as Progressive Multifocal Leukoencephalopathy (PML). **Warnings and Precautions:** 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 institute 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. *Infections:* Entyvio is not recommended in patients with active, severe infections until the infections are controlled. Consider withholding in patients who develop a 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):* No cases were observed in Entyvio clinical trials, but PML a potential fatal opportunistic infection caused by John Cunningham (JC) virus has occurred in patients treated with other integrin receptor antagonists and systemic immunosuppressive agents. Monitor patients for any new or worsening neurological signs/symptoms. *Malignancy:* There is an increased risk of malignancy in UC and CD; immunomodulatory products may increase risk. No increased risk with vedolizumab to date. Long term evaluation ongoing. *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 normally 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. Concomitant administration of corticosteroids, immunomodulators (azathioprine, 6-mercaptopurine, and methotrexate) and aminosalicylates did not have a clinically meaningful effect on Entyvio pharmacokinetics. **Fertility, pregnancy and lactation:** Women of child-bearing potential should use adequate contraception and continue for at least 18 weeks after last Entyvio treatment. Since maternal antibodies are excreted in breast milk, decision whether to discontinue breast-feeding or discontinue/abstain from Entyvio should be made according to relative benefit to child of breast-feeding or to mother of Entyvio. **Undesirable Effects:** *Very Common (>1/10):* nasopharyngitis, headache, arthralgia. *Common (>1/100, <1/10):* bronchitis, gastroenteritis, URTI, influenza, sinusitis, pharyngitis, paraesthesia, hypertension, oropharyngeal pain, nasal congestion, cough, anal abscess, anal fissure, nausea, dyspepsia, constipation, abdominal distension, flatulence, haemorrhoids, rash, pruritis, eczema, erythema, night sweats, acne, muscle spasm, back pain, muscular weakness, fatigue, pyrexia. Other serious undesirable effects: respiratory tract infection, infusion site reaction, infusion-related reaction. **Refer to the SmPC for details on full side effect profile and interactions. Pharmacotherapeutic Classification:** Immunosuppressive, Selective Immunosuppressive, ATC-Code: L04AA33. **Marketing Authorisation Holder:** Takeda Pharma A/S, Dybendal Alle 10, 2630 Taastrup, Denmark. **PI Approval Code:** UK/EYV/1405/0015. **Date of revision:** June 2014

Adverse events should be reported to the authorities in your country as required by local law. Adverse events should also be reported to Takeda at eupv@tgrd.com

Reference: 1. Entyvio® (vedolizumab) Summary of Product Characteristics. June 2014. Last accessed January 2015.

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