Entyvio® (vedolizumab) PRESCRIBING INFORMATION

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

Presentation: Entyvio IV: 300 mg powder for concentrate for solution for infusion. **Entyvio S/C**: 108mg solution for injection in pre-filled syringe or pen. **Indication:** 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. **Dosage & Administration:** Treatment should be initiated and supervised by a specialist healthcare professional experienced in diagnosis and treatment of UC or CD. **Entyvio IV:** Patients should be monitored during and after infusion in a setting equipped to manage anaphylaxis. UC: Recommended dose regimen 300mg administered by IV infusion over 30 minutes at 0, 2, 6 weeks and 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 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. CD: Recommended dose regimen is 300mg administered by IV infusion over 30 minutes at 0, 2, 6 weeks and 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. **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 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 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. **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. 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. 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 effect on infants is 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), bronchitis, gastroenteritis, upper respiratory tract infection, influenza, sinusitis, pharyngitis, paraesthesia, hypertension, oropharyngeal pain, nasal congestion, cough, anal abscess, anal fissure, nausea, dyspepsia, constipation, abdominal distension, flatulence, haemorrhoids, rash, pruritus, eczema, erythema, night sweats, acne, muscle spasm, back pain, muscular weakness, fatigue, pain in extremities, pyrexia. Other serious undesirable effects: respiratory tract infection, pneumonia, anaphylactic reaction, anaphylactic shock. **Refer to the SmPC for details on full side effect profile and interactions. UK Basic NHS Price: Entyvio IV:** £2,050 for one vial (300mg powder for concentrate for solution for infusion). **Entyvio S/C:** £512.50 for one pre-filled syringe or pen. **Legal Classification:** POM. **Marketing Authorisation:** EU/1/14/923/001. **Entyvio S/C:** EU/1/14/923/002, EU/1/14/923/003, EU/1/14/923/005, EU/1/14/923/006. **Name and Address of MA holder:** Takeda UK Ltd. 1 Kingdom Street, London, W2 6BD. Takeda Products Ireland Ltd. 5 Riverwalk, Citywest Business Campus, Dublin 24, D24 TW13. **PI Approval Code**: pi-00820 **Date of revision:** April 2020.

UK: Adverse events should be reported to the Medicines and Healthcare products Regulatory Agency. Reporting forms and information can be found at https://yellowcard.mhra.gov.uk/. Adverse events should also be reported and additional information on our products is available on request from Takeda UK Ltd. DSO-UK@takeda.com

Ireland: Adverse Events should be reported to the Pharmacovigilance Unit at the Health Products Regulatory Authority (medsafety@hpra.ie). Information about Adverse Event reporting can be found on the HPRA website (www.hpra.ie). Adverse events should also be reported and additional information on our products is available on request from Takeda UK Ltd. DSO-UK@takeda.com