FDA APPROVES TAKEDA’S ENTYVIO™ (VEDOLIZUMAB) FOR THE TREATMENT OF ADULTS WITH MODERATELY TO SEVERELY ACTIVE ULCERATIVE COLITIS OR CROHN’S DISEASE

Deerfield, Ill., and Osaka, Japan—Takeda Pharmaceutical Company Limited (“Takeda”) and its wholly-owned subsidiary, Takeda Pharmaceuticals U.S.A., Inc., today announced that the United States (U.S.) Food and Drug Administration (FDA) simultaneously approved a new biologic therapy, Entyvio™ (vedolizumab), for the treatment of adults with moderately to severely active ulcerative colitis (UC) and Crohn’s disease (CD).

“Entyvio is a new option that works to block important contributors to the chronic inflammation that is a hallmark of ulcerative colitis and Crohn’s disease,” said Stephen B. Hanauer, M.D., medical director, Digestive Health Center, Northwestern University Feinberg School of Medicine. “The clinical trial program evaluated the efficacy and safety profile of Entyvio and demonstrated that Entyvio has the potential to help adult patients with moderately to severely active UC or CD successfully manage their disease.”

Entyvio is now approved for inducing and maintaining clinical response and remission, improving endoscopic appearance of the mucosa, and achieving corticosteroid-free remission in adult patients with moderately to severely active UC who have had an inadequate response with, lost response to, or were intolerant to a tumor necrosis factor (TNF) blocker or immunomodulator; or had an inadequate response with, were intolerant to, or demonstrated dependence on corticosteroids. Entyvio is also approved for achieving clinical response and remission, and achieving corticosteroid-free remission in adult patients with moderately to severely active CD who have had an inadequate response with, lost response to, or were intolerant to a TNF blocker or immunomodulator; or had an inadequate response with, were intolerant to, or demonstrated dependence on corticosteroids.

“Patients with moderately to severely active ulcerative colitis or Crohn’s disease, and the healthcare professionals who care for them, need additional new treatment options,” said Douglas Cole, president, Takeda Pharmaceuticals U.S.A., Inc. “Entyvio reflects an expansion of Takeda’s commitment to supporting patients with gastrointestinal disorders.”

The Entyvio dose regimen is 300 mg infused intravenously over approximately 30 minutes at zero, two and six weeks, then every eight weeks thereafter.

Patients should be observed during infusion and until the infusion is complete. See dosage and administration section in full prescribing information.

In March, Entyvio received a positive Opinion for the treatment of adults with moderately to severely active UC and CD from the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA), and Takeda is awaiting response from the European Commission on approval for Marketing Authorisation.

**Clinical Trial Program**

The Biologics License Application filing with the FDA was supported by the largest Phase 3 clinical trial program conducted to date simultaneously evaluating both UC and CD patient populations in four clinical studies involving 2,700 patients in nearly 40 countries. Three of these studies were randomized, double-blind, placebo-controlled trials – GEMINI I (UC Trials I and II), GEMINI II (CD Trials I and III) and GEMINI III (CD Trial II). GEMINI I, II and III evaluated adult patients with moderately to severely active UC or CD who had an inadequate response or intolerance to TNF blocker or immunomodulator therapy; inadequate response, loss of response, or intolerance to a TNF blocker; or were corticosteroid dependent or had an inadequate response or intolerance to corticosteroids.

Adverse reactions were reported in 52 percent of patients treated with Entyvio and 45 percent of patients treated with placebo (UC Trials I and II: 49 percent with Entyvio and 37 percent with placebo; CD Trials I and III: 55 percent with Entyvio and 47 percent with placebo). Serious adverse reactions were reported in 7
percent of patients treated with Entyvio compared to 4 percent of patients treated with placebo (UC Trials I and II: 8 percent with Entyvio and 7 percent with placebo; CD Trials I and III: 12 percent with Entyvio and 9 percent with placebo).

The most common adverse reactions reported with Entyvio (incidence greater than or equal to 3 percent and greater than or equal to 1 percent higher than placebo) were nasopharyngitis, headache, arthralgia, nausea, pyrexia, upper respiratory tract infection, fatigue, cough, bronchitis, influenza, back pain, rash, pruritus, sinusitis, oropharyngeal pain, and pain in extremities.

About Entyvio™ (vedolizumab)

Entyvio, an integrin receptor antagonist, is a humanized monoclonal antibody that specifically binds to the alpha4beta7 integrin and blocks the interaction of alpha4beta7 integrin with mucosal addressin cell adhesion molecule-1 (MAdCAM-1) and inhibits the migration of memory T-lymphocytes across the endothelium into inflamed gastrointestinal parenchymal tissue. Entyvio does not bind to or inhibit function of the alpha4beta1 and alpha E beta 7 integrins and does not antagonize the interaction of alpha4 integrins with vascular cell adhesion molecule-1 (VCAM-1). The alpha4beta7 integrin is expressed on the surface of a discrete subset of memory T-lymphocytes that preferentially migrate into the gastrointestinal tract. MAdCAM-1 is mainly expressed on gut endothelial cells and plays a critical role in the homing of T-lymphocytes to gut lymph tissue. The interaction of the alpha4beta7 integrin with MAdCAM-1 has been implicated as an important contributor to the chronic inflammation that is a hallmark of ulcerative colitis and Crohn’s disease.

INDICATIONS: ENTYVIO™ (vedolizumab)

**Adult Ulcerative Colitis (UC)**

Adult patients with moderately to severely active UC who have had an inadequate response with, lost response to, or were intolerant to a tumor necrosis factor (TNF) blocker or immunomodulator; or had an inadequate response with, were intolerant to, or demonstrated dependence on corticosteroids:

- inducing and maintaining clinical response
- inducing and maintaining clinical remission
- improving endoscopic appearance of the mucosa
- achieving corticosteroid-free remission

**Adult Crohn’s Disease (CD)**

Adult patients with moderately to severely active CD who have had an inadequate response with, lost response to, or were intolerant to a TNF blocker or immunomodulator; or had an inadequate response with, were intolerant to, or demonstrated dependence on corticosteroids:

- achieving clinical response
- achieving clinical remission
- achieving corticosteroid-free remission

**IMPORTANT SAFETY INFORMATION**

- **ENTYVIO (vedolizumab)** is contraindicated in patients who have had a known serious or severe hypersensitivity reaction to ENTYVIO or any of its excipients.
- Infusion-related reactions and hypersensitivity reactions including anaphylaxis have occurred. If anaphylaxis or other serious allergic reactions occur, discontinue administration of ENTYVIO immediately and initiate appropriate treatment.
- Patients treated with ENTYVIO are at increased risk for developing infections. Serious infections have been reported in patients treated with ENTYVIO. ENTYVIO is not recommended in patients with active, severe infections until the infections are controlled. Consider withholding ENTYVIO in patients who develop a severe infection while on treatment with ENTYVIO. Exercise caution in patients with a history of recurring severe infections.
- Although no cases of PML have been observed in ENTYVIO clinical trials, JC virus infection resulting in progressive multifocal leukoencephalopathy (PML) and death has occurred in patients treated with another integrin receptor antagonist. A risk of PML cannot be ruled out. Monitor patients for any new or worsening neurological signs or symptoms. If PML is suspected, withhold dosing with ENTYVIO and refer to a neurologist; if confirmed, discontinue ENTYVIO dosing permanently.
- There have been reports of elevations of transaminase and/or bilirubin in patients receiving ENTYVIO. ENTYVIO should be discontinued in patients with jaundice or other evidence of significant liver injury.
- Prior to initiating treatment with ENTYVIO, all patients should be brought up to date with all immunizations according to current immunization guidelines. Patients receiving ENTYVIO may receive non-live vaccines and may receive live vaccines if the benefits outweigh the risks.
- Most common adverse reactions (incidence greater than or equal to 3% and greater than or equal to 1% higher than placebo): nasopharyngitis, headache, arthralgia, nausea, pyrexia, upper respiratory tract infection, fatigue, cough, bronchitis, influenza, back pain, rash, pruritus, sinusitis, oropharyngeal pain, and pain in extremities.

Please see the accompanying full Prescribing Information including Medication Guide for ENTYVIO. More information will also be available soon at: [www.ENTYVIOHCP.com](http://www.ENTYVIOHCP.com) and [www.ENTYVIO.com](http://www.ENTYVIO.com)