Recommendations

- Consider the patient's full medical history, including any prior or concurrent biological medicine use
- There is no clinical trial experience with ENTYVIO in patients previously treated with natalizumab. Given the known risk of PML development in patients with previous natalizumab exposure, physicians should normally wait 12 weeks after the last natalizumab dose prior to initiating ENTYVIO treatment.
- Patients treated with ENTYVIO should be monitored for any new onset or worsening of neurological signs and symptoms such as those listed below:
    - Progressive weakness on one side of the body or clumsiness of limbs
    - Disturbance of vision
    - Changes in thinking, memory, and orientation, leading to confusion and personality changes
- Any patients with new onset or worsening signs and symptoms suggestive of PML should be considered for neurological referral at a center equipped to diagnose PML.

Entyvio™ vedolizumab

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Important Safety Information

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Using ENTIVYO for Patients with Ulcerative Colitis or Crohn's Disease

▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. Report form can be downloaded from www.medicinesauthority.gov.mt/adrportal and sent by post or email to;
P: Medicines Authority, Sir Temi Zammit Buildings, Malta Life Sciences Park, San Gwann SGN 3000, Malta
E: postlicensing.medicinesauthority@gov.mt

ENTYVIO (vedolizumab) is a gut-selective, humanized monoclonal antibody that is indicated for use in adult patients with either moderately to severely active ulcerative colitis (UC) or Crohn's disease (CD) who had an inadequate response with, lost response to, or were intolerant to either conventional UC or CD therapies or a tumor necrosis factor-alpha (TNFα) antagonist.

IMPORTANT SAFETY INFORMATION

Progressive multifocal leukoencephalopathy (PML) is a rare and often fatal opportunistic infection of the central nervous system that has been associated with the use of TYSABRI® (natalizumab, a α4β7 and α4β1 integrin antagonist), which is indicated for use in patients with multiple sclerosis. It is hypothesized that the risk for PML with natalizumab is primarily due to binding to the α4β1 integrin which inhibits leukocyte migration and immunosurveillance of the CNS and not the binding to the α4β7 integrin which inhibits migration of certain leukocytes to the gastrointestinal tract. However, the theoretical risk of PML with ENTYVIO cannot be excluded because ENTYVIO binds to the α4β7 integrin.

At the approval of vedolizumab, no cases of PML occurred in over 3100 patients treated with ENTYVIO in clinical trials. There is no evidence of systemic or CNS immunosuppression with ENTYVIO. However, the theoretical risk of a patient treated with ENTYVIO developing PML cannot be excluded. Therefore, patients treated with ENTYVIO should be monitored for any new onset or worsening of neurological symptoms such as those listed below:

- Progressive weakness on one side of the body or clumsiness of limbs
- Disturbance of vision
- Changes in thinking, memory, and orientation, leading to confusion and personality changes

Any patients with new or worsening signs and symptoms suggestive of PML should be considered for neurological referral at a center equipped to diagnose PML. If PML is suspected, treatment with ENTYVIO must be withheld; and if confirmed, treatment must be permanently discontinued. Suspected cases of PML should be reported to Takeda or directly to Medicines Authority.

Considerations before treating patients with previous natalizumab exposure

There is no clinical trial experience with ENTYVIO in patients previously treated with natalizumab. Since natalizumab has been associated with an increased risk of PML, physicians should normally wait 12 weeks after the last natalizumab dose prior to initiating treatment with ENTYVIO.

Physicians are encouraged to enroll patients into the Takeda-sponsored study to observe and evaluate long-term safety in patients with UC or CD. Please contact Entyvio401study@entyviopass.com

Prescribing ENTYVIO

ENTYVIO is administered as an intravenous infusion over 30 minutes and must be reconstituted and diluted prior to administration. ENTYVIO should not be administered intramuscularly or as an intravenous push or bolus.

Prior to treatment initiation patients should be advised on the potential benefits and risks of ENTYVIO. Patients should be provided the Patient Information Leaflet and the patient Alert Card for ENTYVIO and have the opportunity to read and ask questions. It is important that the patient's overall health be assessed at each infusion visit and any questions resulting from the patient's reading of the Patient Information Leaflet be discussed.

There is no clinical trial experience in patients concomitantly receiving biologic immunosuppressants. Therefore, the use of Vedolizumab Takeda in such patients is not recommended

Reporting Suspected Adverse Reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in the product information.

Long-term Observational Safety Study Information

Takeda is sponsoring a voluntary long-term observational safety study enrolling patients with UC or CD on biologic therapy to observe and evaluate long-term safety. You are encouraged to enroll patients who are initiating ENTYVIO, or similar patients who are initiating another biologic, particularly those who have been previously treated with natalizumab.

Please contact Entyvio401study@entyviopass.com

Please see the accompanying full Prescribing Information and Medication Guide.

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