MAYO CLINIC LABORATORIES

# Test Definition: VEDOL

Vedolizumab Quantitation with Reflex to Antibodies, Serum

## Overview

### Useful For

Evaluation of patients with loss of response to vedolizumab (VDZ) with recurrence of symptoms and/or low or undetectable serum VDZ measured at trough

Monitoring vedolizumab concentrations in patients undergoing therapy with this biologic for ulcerative colitis or Crohn disease

Assessing the loss of response to VDZ therapy

As an aid to achieving desired serum concentration of VDZ

### Reflex Tests

| Test Id | Reporting Name | Available Separately | Always Performed |
|---|---|---|---|
| VEMAB | Vedolizumab Ab, S | No | No |

### Testing Algorithm

Vedolizumab quantitation will be performed by liquid chromatography mass spectrometry on all samples. When this test is ordered and vedolizumab results are 15.0 mcg/mL or less, then testing for antibodies to vedolizumab will be performed at an additional charge.

This test includes vedolizumab drug quantitation and, if appropriate, antibody testing for antibodies-to-vedolizumab will be performed. Currently, the American Gastroenterology Association does not have a formal guideline on optimal thresholds for vedolizumab trough concentrations in the setting of loss of response to therapy, but trough concentrations greater than 15 mcg/mL have been associated with clinical or endoscopic remission and mucosal healing in inflammatory bowel disease.

For more information see Ulcerative Colitis and Crohn Disease Therapeutic Drug Monitoring Algorithm.

### Special Instructions

- Ulcerative Colitis and Crohn Disease Therapeutic Drug Monitoring Algorithm

### Method Name

VEDOL: Liquid Chromatography Mass Spectrometry (LC-MS/MS)
VEMAB: Electrochemiluminescent Bridging Immunoassay

### NY State Available

Yes

## Specimen

### Specimen Type
Serum

### Ordering Guidance
If both quantitation and antibody testing are needed, regardless of the quantitation results, order VEDOZ / Vedolizumab Quantitation with Antibodies, Serum.

### Specimen Required
**Patient Preparation:** For 12 hours before specimen collection, patient **should not** take multivitamins or dietary supplements (eg, hair, skin, and nail supplements) containing biotin (vitamin B7).
**Supplies:** Sarstedt Aliquot Tube, 5 mL (T914)
**Collection Container/Tube:**
**Preferred:** Red top
**Acceptable:** Serum gel
**Submission Container/Tube:** Plastic vial
**Specimen Volume:** 1.5 mL Serum
**Collection Instructions:**
1. Draw blood immediately before next scheduled dose (trough specimen).
2. Within 2 hours of collection, centrifuge and aliquot serum into a plastic vial.

### Forms
If not ordering electronically, complete, print, and send 1 of the following with the specimen:
-Gastroenterology and Hepatology Test Request (T728)
-Therapeutics Test Request (T831)

### Specimen Minimum Volume
Serum: 0.3 mL

### Reject Due To

| | |
|---|---|
| Gross hemolysis | OK |
| Gross lipemia | OK |
| Gross icterus | OK |

### Specimen Stability Information

| Specimen Type | Temperature | Time | Special Container |
|---|---|---|---|
| Serum | Refrigerated (preferred) | 28 days | |
| | Frozen | 28 days | |

## Clinical & Interpretive

### Clinical Information

Drug and target:
Vedolizumab (VDZ, Entyvio) is a humanized IgG1 kappa monoclonal antibody directed against integrin alpha-4 beta-7 integrin expressed on lymphocytes. VDZ blocks the interaction between the alpha-4 beta-7 integrin and MAdCAM-1, preventing lymphocytes from migrating across the endothelium into inflamed gastrointestinal tissue, thereby reducing inflammation.

Indications:
Vedolizumab is US Food and Drug Administration-approved for the treatment of adult patients with moderately to severely active ulcerative colitis or Crohn disease.(1,2) The standard dosing is 300 mg intravenously (IV) at weeks 0, 2, and 6 (induction), and then every 8 weeks for maintenance. It may be given every 4 weeks in certain cases of partial response.

Pharmacokinetic highlights:
Steady-state trough concentrations are typically achieved after the first few maintenance doses (around 14-22 weeks into therapy). Another option is subcutaneous injection with 108 mg every 2 weeks for maintenance after initial IV induction at weeks 0 and 2. The reported median steady state trough serum concentrations range from 19 to 48 mcg/mL, with multiple studies demonstrating an increase of at least 10 mcg/mL after transition from IV to subcutaneous administration.(3-9)

Immunogenicity:
Patients on VDZ may develop antibodies to VDZ (ATV) over time. In clinical trials, approximately 4% of patients treated with VDZ were positive for ATV at any time and 1% or less had specimens that were persistently positive. ATV formation may increase drug clearance in treated patients and/or neutralize the drug effect, thereby potentially contributing to the loss of response. ATV could also cause adverse events such as serum sickness and hypersensitivity reactions. VDZ drug level quantitation is commonly performed in conjunction with immunogenicity assessment for ATV.

Evidence for therapeutic drug monitoring:
Optimal therapeutic concentrations of VDZ associated with clinical remission and mucosal healing range between 12 and 28 mcg/mL, depending on the stage of therapy (induction or maintenance).(10-13) Most often, testing is ordered for patients on therapy who are experiencing loss of response (reactive monitoring). In the setting of loss of response to therapy, testing for ATV may be performed as a reflex after the drug quantitation shows subtherapeutic levels of VDZ (this test) or as a panel where drug quantitation and ATV are performed simultaneously (VEDOZ / Vedolizumab Quantitation with Antibodies, Serum). Results from drug quantitation combined with ATV testing play an important role in patient management.(10,12,13)

Proactive monitoring of ATV in a patient who is responding to therapy with VDZ is not recommended by the American Gastroenterology Association.

### Reference Values

VEDOLIZUMAB QUANTITATION:

Vedolizumab lower limit of quantitation: 1.0 mcg/mL

VEDOLIZUMAB ANTIBODIES:
Antibodies to vedolizumab: <9.8 ng/mL

Absence of antibodies to vedolizumab is defined as <9.8 ng/mL
Presence of ATV is reported as positive when concentrations are > or =9.8 ng/mL

## Interpretation

Unlike anti-tumor necrosis factor agents, the American Gastroenterology Association has not set formal target concentrations for vedolizumab. However, experts acknowledge that vedolizumab trough concentrations greater than 15 mcg/mL are associated with better outcomes in inflammatory bowel disease (IBD), with an association between higher vedolizumab concentration and clinical remission in IBD. European Crohn's and Colitis Organization guidance suggests considering intensification if the trough result is less than 20 mcg/mL in active disease.

In summary, current consensus is that vedolizumab therapeutic drug monitoring is useful reactively, and that trough results greater than or equal to 15 mcg/mL are desirable for optimal response, although an official "therapeutic range" is not firmly established. In a retrospective Mayo Clinic study with 171 patients (62% Crohn disease, 31% ulcerative colitis, and 7% indeterminate colitis), the median vedolizumab trough concentration was 15.3 mcg/mL. VDZ concentration greater than 15 mcg/mL at trough was associated with clinical remission, endoscopic remission, or mucosal healing in IBD.

Clinically significant antibodies to vedolizumab (ATV) impact drug clearance and are associated with low or undetectable vedolizumab concentration. Presence of ATV is associated with poorer outcomes and increased VDZ clearance.

Table. Interpretation

| Vedolizumab quantitation mcg/mL | Antibodies to vedolizumab ng/mL | Comment |
|---|---|---|
| <15 | <9.8 | Absence of detectable antibodies to vedolizumab (ATV). Low or undetectable concentration of vedolizumab (VDZ) may be attributable to other parameters related to VDZ clearance. |
| > or =15 | <9.8 | Absence of detectable ATV. VDZ concentration is associated with clinical remission, endoscopic remission, or mucosal healing in inflammatory bowel disease.<br>In the presence of symptoms, this finding would suggest mechanistic failure.<br><br>At this concentration of VDZ, a low-titer ATV cannot be completely excluded. However, the presence of a high-titer ATV is unlikely. |

| | | |
|---|---|---|
| | | If there is clinical suspicion for a low-titer ATV, suggest submission of a new sample obtained at trough. |
| <15 | > or =9.8 | Presence of ATV detected, which may correlate with low or undetectable concentration of VDZ. ATVs may be associated with increased clearance and lower circulating concentrations of VDZ. |
| > or =15 | > or =9.8 | Presence of ATV detected. In the presence of symptoms, this finding would suggest mechanistic failure and immunogenicity. |

## Cautions

The presence of high concentrations of vedolizumab might inhibit the antibodies to vedolizumab (ATV) assay yielding false-negative results. In patients with concentrations of vedolizumab greater than 15.0 mcg/mL, the presence of an ATV is of little clinical significance.

Specimens containing more than 100 ng/mL biotin (vitamin B7) may interfere (in the form of depressed signal) with VEMAB / Vedolizumab Antibodies, Serum. It is recommended patients stop taking biotin-containing vitamins or supplements 12 hours before specimen collection.

Clinical management decisions for patients receiving vedolizumab treatment should not be based solely on quantitation of vedolizumab and assessment of ATV if appropriate. Test results must be interpreted within the clinical context of the patient.

The test measures vedolizumab drug concentration specifically. When biosimilars for vedolizumab become available, the assay would be expected to detect them as they have the same molecular structure. The report would likely note it cannot distinguish Entyvio from a biosimilar. Currently, this is not applicable.

## Clinical Reference

1. Feagan BG, Rutgeerts P, Sands BE, et al. Vedolizumab as induction and maintenance therapy for ulcerative colitis. N Engl J Med. 2013;369(8):699-710
2. Chan AD, Carter PJ. Therapeutic antibodies for autoimmunity and inflammation. Nat Rev Immunol. 2010;10(5):301-316. doi:10.1038/nri2761
3. Sandborn WJ, Baert F, Danese S, et al. Efficacy and safety of Vedolizumab subcutaneous formulation in a randomized trial of patients with ulcerative colitis. Gastroenterology. 2020;158(3):562–572.e12.
4. Vermeire S, D'Haens G, Baert F, et al. Efficacy and safety of subcutaneous Vedolizumab in patients with moderately to severely active Crohn's disease: Results from the VISIBLE 2 randomised trial. J. Crohns Colitis. 2022;16(1):27-38
5. Volkers A, Straatmijer T, Duijvestein M, et al. Real-world experience of switching from intravenous to subcutaneous Vedolizumab maintenance treatment for inflammatory bowel diseases. Aliment Pharmacol. Ther. 2022;56(6):1044-1054
6. Wiken TH, Hoivik ML, Buer L, et al. Switching from intravenous to subcutaneous vedolizumab maintenance treatment in patients with inflammatory bowel disease followed by therapeutic drug monitoring. Scand J Gastroenterol. 2023;58(8):863-873
7. Bergqvist V, Holmgren J, Klintman D, et al. Real-world data on switching from intravenous to subcutaneous

vedolizumab treatment in patients with inflammatory bowel disease. Aliment Pharmacol. Ther. 2022;55(11):1389-1401
8. Ventress E, Young D, Rahmany S, et al. Transitioning from Intravenous to Subcutaneous Vedolizumab in Patients with Inflammatory Bowel Disease [TRAVELESS]. J Crohns Colitis. 2022;16(6):911-921
9. Orsic Fric V, Borzan V, Sahinovic I, et al. Real-world study on Vedolizumab serum concentration, efficacy, and safety after the transition from intravenous to subcutaneous vedolizumab in inflammatory bowel disease patients: single-center experience. Pharmaceuticals (Basel). 2023;16(2):239
10. Cradic KW, Ladwig PM, Rivard AL, Katrangi W, Wintgens KF, Willrich MAV. Vedolizumab quantitation using high-resolution accurate mass-mass spectrometry middle-up protein subunit: method validation. Clin Chem Lab Med. 2020;58(6):864-72
11. Al-Bawardy B, Ramos GP, Willrich MAV, et al. Vedolizumab drug level correlation with clinical remission, biomarker normalization, and mucosal healing in inflammatory bowel disease. Inflamm Bowel Dis. 2019;25(3):580-586
12. Dulai PS, Amiot A, Peyrin-Biroulet L, et al. A clinical decision support tool may help to optimise vedolizumab therapy in Crohn's disease. Aliment Pharmacol Ther. 2020;51(5):553-64
13. Dreesen E, Verstockt B, Bian S, et al. Evidence to support monitoring of vedolizumab trough concentrations in patients with inflammatory bowel diseases. Clin Gastroenterol Hepatol. 2018;16(12):1937-46 e8
14. Papamichael K, Cheifetz AS, Melmed GY, et al. Appropriate therapeutic drug monitoring of biologic agents for patients with inflammatory bowel diseases. Clin Gastroenterol Hepatol. 2019;17(9):1655-68 e3

## Performance

### Method Description

Vedolizumab quantitation:
Vedolizumab is extracted from serum and measured by liquid chromatography (high-resolution accurate-mass, HRAM) mass spectrometry.(Unpublished Mayo method)

Vedolizumab antibodies:
Testing for antibodies to vedolizumab is performed using a laboratory-developed immunoassay.(Unpublished Mayo method)

### PDF Report

No

### Day(s) Performed

Monday, Wednesday, Thursday

### Report Available

5 to 7 days

### Specimen Retention Time

14 days

### Performing Laboratory Location

Mayo Clinic Laboratories - Rochester Superior Drive

## Fees & Codes

### Fees

- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact Customer Service.

### Test Classification

This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. It has not been cleared or approved by the US Food and Drug Administration.

### CPT Code Information

80280
82397 (if appropriate)

### LOINC® Information

| Test ID | Test Order Name | Order LOINC® Value |
|---|---|---|
| VEDOL | Vedolizumab QN, S | 90805-3 |

| Result ID | Test Result Name | Result LOINC® Value |
|---|---|---|
| 602807 | Vedolizumab QN, S | 90805-3 |