Insurance Company

**RE: PATIENT**

**DOB:**

**ID#**

**Pat Acct #**

Dear Sir, or Madam:

To Whom It May Concern:

I am writing this letter on behalf of my patient, PATIENT NAME, to request that you reconsider your decision to deny payment for the ustekinumab trough test that was performed on \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_.  This test measures the level of ustekinumab and checks for the presence of anti-ustekinumab antibodies.

INSERT PATIENT’s CLNICAL SITUATION AND REASON FOR ODERING TEST HERE

Despite the efficacy of our currently available biologic agents, up to 30% of patients do not respond to their prescribed treatment (primary non-response), and another 50% may ultimately lose response to their treatment over time (secondary loss of response).1,2 A proportion of these patients may be found to have suboptimal drug levels either due to inadequate dosing or development of anti-drug antibodies, the latter which result in increased drug clearance.3 The practice of therapeutic drug monitoring (TDM), through which drug concentrations and the presence of anti-drug antibodies are measured, is a necessary tool used to understand *why* an individual patient is not responding or has lost response to a therapy. The results of such testing can facilitate decision-making, specifically as to whether a specific biologic can be further dose optimized to improve clinical response, or if rather a treatment change to a different biologic would be indicated. This helps to improve clinical outcomes and prevent unnecessary biologic switches. An expert consensus statement was published in 2021 following a comprehensive literature review, supporting the use of TDM for all biologics in the setting of primary non-response and secondary loss of response.4

There is good data to support the use of ustekinumab trough testing in the evaluation of loss of response to therapy. In patients with IBD, measuring ustekinumab trough levels in nonresponders is indicated at post-induction (week 8) and concentrations of ustekinumab associated with more favorable outcomes are more than 3.5 mcg/mL. In the maintenance phase of therapy, ustekinumab concentrations greater than or equal to 1 mcg/mL are associated with clinical response and clinical remission, while concentrations greater than or equal to 4.5 mcg/mL are associated with mucosal healing.5 Additionally, studies have shown that between 3-5% of IBD patients develop anti-drug antibodies when treated with ustekinumab at one year.5 Thus, it is important to evaluate for the presence of any anti-drug antibodies when evaluating patients who have lost response to this treatment.

In this clinical setting where PATIENT has NOT RESPONDED/LOST RESPONSE to ustekinumab, it was entirely appropriate to pursue TDM in order to determine whether the dose of ustekinumab could be optimized or if we would need to consider switching to a different mechanism of action altogether.  The referenced papers show that therapeutic drug monitoring of biologics is rapidly becoming a standard of care in the field of inflammatory bowel disease.  It is impossible to know confidently how to manage loss of response to ustekinumab without checking trough levels and antibodies first.

Please reconsider this decision to deny payment for the ustekinumab trough test. Feel free to contact me if you require additional information.

Sincerely,

DOCTOR

**CLINICAL REFERENCEs**

1. Vande Casteele N, Herfarth H, Katz J, et al. American Gastroenterological Association institute technical review on the role of therapeutic drug monitoring in the management of inflammatory bowel Diseases. Gastroenterology 2017;153:835–57.
2. Sparrow MP, Papamichael K, Ward MG, et al. Therapeutic drug monitoring of biologics during induction to prevent primary non-response. J Crohns Colitis 2020;14:542–56
3. Vermeire S, Dreesen E, Papamichael K, et al. How, when, and for whom should we perform therapeutic drug monitoring? Clin Gastroenterol Hepatol 2020;18:1291–9.
4. Cheifetz AS, Abreu MR, Afif W, et al. A Comprehensive Literature Review and Expert Consensus Statement on Therapeutic Drug Monitoring of Biologics in Inflammatory Bowel Disease. Am J Gastroenterol. 2021 Oct;116(10):2014-25.
5. 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 Aug;17(9):1655-1668.e3