**Supportive text for statements 1-9**

Reactive therapeutic drug monitoring (TDM) is the evaluation of drug concentration and anti-drug antibodies (ADA) in the setting of treatment failure and can help explain the potential mechanism underlying primary non-response or secondary loss of response to anti-tumor necrosis factor (anti-TNF) therapy and consequently better direct the next step of care. For example, a higher amount of drug should be given to patients with low or undetectable drug concentrations and no ADA, whereas switching drug is recommended for patients with high-titer ADA, and switching drug class is recommended for patients with adequate drug concentrations.6-9 Though reactive TDM is recommended by many medical societies high quality data from randomized controlled trials (RCTs) using objective endpoints are missing.10 Moreover, reactive TDM compared to clinical symptoms alone has been proven more cost-effective to guide therapeutic decisions in patients with inflammatory bowel disease (IBD) treated with infliximab.27 Nevertheless, emphasis should be given on confirming there is a link between measurement of drug concentrations/ADA with objective disease activity assessments (i.e. endoscopic/calprotectin) to ensure inappropriate and costly dose escalation is not undertaken.

When treating patients with IBD, and particularly when performing reactive TDM it is of great clinical significance to optimize the first biologic as this typically offers a higher rate of efficacy when compared to subsequent biologic therapies.28, 29 Moreover, there are still limited pharmacological options for IBD, particularly for certain phenotypes. Infliximab, for example, continues to be the cornerstone pharmacological treatment in acute severe ulcerative colitis (UC) and perianal fistulizing Crohn’s disease (CD). Thus, treatment discontinuation should not be considered until an infliximab concentration of at least 10-15μg/ml is achieved. Similarly, treatment discontinuation should not be considered for adalimumab until a drug concentration of at least 10-15μg/ml is achieved. However, it should be noted, there may be some instances where these drug concentrations may not be achievable for various reasons including high drug clearance and lack of insurance approval for dose escalation.

At this time, the vast majority of the data on reactive TDM relates to anti-TNFs. For non anti-TNF biologics the only current evidence supporting the role of reactive TDM is derived mostly from exposure-response relationship studies showing that higher vedolizumaband ustekinumabconcentrations are associated with better therapeutic outcomes.30-44

**Supportive text for statement 22**

Current data suggest that there are no differences in performing and interpreting the results of TDM between the infliximab biosimilars SB2 and CT-P13 and the originator drug using commercially available enzyme-linked immunosorbent assays (ELISAs).78-80

**Supportive text for statements 40 and 41**

A study from Vande Casteele et al. identified (using an ELISA) a certolizumab pegol concentration cut-off of 31.9 μg/mL, 32.7 μg/mL and 34.5 μg/mL at week 6 for C-reactive protein (CRP) ≤5mg/L, fecal calprotectin (FC) <250μg/g and combined FC <250μg/g and Crohn’s disease activity index (CDAI) ≤150 at week 6, respectively, in patients with CD.117 The same study identified a certolizumab pegol concentration cut-off of 13.8 μg/mL and 14.8 μg/mL at week 12 for FC<250μg/g and combined FC <250μg/g and CDAI≤150 at week 26, respectively.117

**Supportive text for statements 42 and 43.**

The GO-LEVEL (Study of the Golimumab Exposure-Response Relationship Using Serum Trough Levels) open label, phase IV study that included a prospective as well as a cross-sectional cohort of patients with UC receiving maintenance golimumab treatment identified (using an ELISA) a golimumab concentration cut-off of 3.2 μg/mL and 3.8 μg/mL at week 6 for clinical [simple clinical colitis activity index (SCCAI ≤2)] remission and combined clinical-biochemical remission (SCCAI ≤2 and FC <250μg/g) at week 6, respectively.118 The same study identified a golimumab concentration cut-off of 2.4 μg/mL for clinical and biochemical remission during maintenance therapy.118 A post-hoc analysis of the PURSUIT (A study to Evaluate the Safety and Efficacy of Golimumab Maintenance Therapy, Administered Subcutaneously, in Subjects With Moderately to Severely Active Ulcerative Colitis) studies identified [using the Janssen electrochemiluminescent immunoassay (ECLIA)] a golimumab concentration cut-off of 2.5 μg/mL at week 6 for clinical response at week 6.S1 The same studyidentified a golimumab concentration cut-off of 0.9 μg/mL at week 28 and 1.4 μg/mL at week 44 for clinical remission at week 54.S1 A study by Dreesen et al. in patients with UC identified (using an in-house ELISA) a golimumab concentration cut-off of 7.4 μg/mL at week 6 and 3.2 μg/mL at week 14 for endoscopic remission (Mayo endoscopic score <2) at week 14.S2

**Supportive text for statements 44-46**

A Propensity-score-based case-matching analysis using data from GEMINI 1 [A Study of Vedolizumab (MLN0002) in Patients With Moderate to Severe Ulcerative Colitis] and an earlier large population pharmacokinetic study showed that potential target vedolizumab concentrations at weeks 6, 14 and steady state (measured by an in-house ELISA) were 37.1, 18.4 and 12.7 µg/mL, respectively.37 A prospective study including 101 patients with IBD identified (using an ELISA) a vedolizumab concentration cut-off of 29.9 μg/mL at week 6 for clinical remission at week 14.S3 The same study identified a vedolizumab concentration cut-off of 16.6 μg/mL at week 14 for drug persistence within the first year of therapy.S3 The prospective LOVE-CD (A Study to Evaluate Efficacy, of Early Versus Late Use of Vedolizumab in Crohn's Disease) study identified (using an ELISA) a vedolizumab concentration cut-off of 10 μg/mL at week 22 for endoscopic remission at week 26.S4 A large cross-sectional multi-centre study of patients with IBD on maintenance vedolizumab therapy identified [using the homogenous mobility shift assay (HMSA)] a vedolizumab concentration cut-off of 11.5 μg/mL and 14.8 μg/mL for corticosteroid-free combined clinical and biochemical remission and for corticosteroid-free deep remission, respectively.32

**Supportive text for statements 47 and 48**

The UNITI (A Study to Evaluate the Safety and Efficacy of Ustekinumab Induction Therapy in Subjects With Moderately to Severely Active Crohn’s Disease) RCT regarding maintenance therapy (using the Janssen ECLIA) identified an ustekinumab concentration cut-off of 0.8 μg/ml at week 24 and 1.4 μg/ml at week 40 for clinical remission at weeks 24 and 44, respectively.43 The same study identified an ustekinumab concentration cut-off of 3.3 μg/ml at week 8 for clinical remission at week 8.43 The UNIFI (A Study to Evaluate the Safety and Efficacy of Ustekinumab Induction Therapy in Subjects With Moderately to Severely Active Ulcerative Colitis) RCT regarding maintenance therapy (using the Janssen ECLIA) identified an ustekinumab concentration cut-off of 1.1 μg/ml and 1.3 μg/ml during maintenance therapy for endoscopic and histologic improvement at week 44, respectively.41 The same study identified an ustekinumab concentration cut-off of 3.5 μg/ml and 3.7 μg/ml at week 8 for endoscopic and histologic improvement at week 8, respectively.41 The prospective study by Verstockt et al. (using an in-house ELISA) identified an ustekinumab concentration cut-off of 2.3 μg/ml at week 16 and 1.9 μg/ml at week 24 for endoscopic response at week 24.33 The same study identified an ustekinumab concentration cut-off of 4.2 μg/ml and 7.2 μg/ml at week 8 for 50% decrease in FC and biological remission at week 8, respectively.33 The study by Battat et al. (using the HMSA) in a combined cohort of patients [a longitudinal cohort prospectively received ustekinumab 90 mg subcutaneous (SC) induction at weeks 0, 1, and 2, followed by ustekinumab 90 mg SC maintenance Q8 weeks and a cross-sectional cohort] identified an ustekinumab concentration cut-off of 4.5 μg/ml at 26 weeks or later for biomarker reduction and endoscopic response.42 A prospective study including patients with CD identified (using an ELISA) an ustekinumab concentration cut-off of 1.1 μg/ml at week 12 for biological response at month 6.S5 Another prospective study in CD identified (using an ELISA) an ustekinumab concentration cut-off of 2 μg/ml at week 8 and 1.4 μg/ml at week 16 for composite remission (Harvey-Bradshaw Index ≤4, CRP<5mg/L and FC<250μg/g) at week 16.S6 Finally, a prospective study by Hanžel et al. in CD identified (using an ELISA) an ustekinumab concentration cut-off of 6.9 μg/ml and 11.1 μg/ml at week 8 for FC<100μg/g and endoscopic remission at week 24, respectively.39

**Supplementary References**

S1. Adedokun OJ, Xu Z, Marano CW, et al. Pharmacokinetics and exposure-response relationship of golimumab in patients with moderately-to-severely active ulcerative colitis: results from phase 2/3 PURSUIT induction and maintenance studies. J Crohns Colitis. 2017;11:35-46.

S2. Dreesen E, Kantasiripitak W, Detrez I, et al. A population pharmacokinetic and exposure-response model of golimumab for targeting endoscopic remission in patients with ulcerative colitis. Inflamm Bowel Dis 2020;26:570-580.

S3. Guidi L, Pugliese D, Tonucci TP, et al. Early vedolizumab trough levels predict treatment persistence over the first year in inflammatory bowel disease. United European Gastroenterol J 2019;7:1189-1197.

S4. Löwenberg M, Vermeire S, Mostafavi N, et al. Vedolizumab induces endoscopic and histologic remission in patients with Crohn's disease. Gastroenterology 2019;157:997-1006.

S5. Painchart C, Brabant S, Duveau N, et al. Ustekinumab serum trough levels may identify suboptimal responders to ustekinumab in Crohn's disease. Dig Dis Sci 2020;65:1445-1452.

S6. Soufflet N, Boschetti G, Roblin X, et al. Concentrations of ustekinumab during induction therapy associate with remission in patients with Crohn's disease. Clin Gastroenterol Hepatol 2019;17:2610-2612.