Therapeutic Drug Monitoring in Adolescents and Children With Inflammatory Bowel Disease

Samantha Saul, MD, MS,[1] John J. DeCaro III, MD,[1] and Jeremy Adler, MD, MSc[1,2]

[1]Pediatric Gastroenterology, Michigan Medicine, University of Michigan, Ann Arbor, Michigan

[2]Susan B. Meister Child Health Evaluation and Research Center, University of Michigan, Ann Arbor, Michigan

Corresponding author:
Jeremy Adler, MD, MSc
2800 Plymouth Road
NCRC Building 16, G029W
Ann Arbor, MI 48109
Tel: (734) 763-9650
Fax: (734) 763-7359
E-mail: jeradler@med.umich.edu

Abstract: Proactive longitudinal therapeutic drug monitoring (TDM) is the standard of care for pediatric patients with inflammatory bowel disease (IBD). This is important because children and adolescents have variable pharmacokinetics as they grow with more rapid drug clearance, most notably in younger and smaller patients. They also commonly have more aggressive disease with higher tissue cytokine burden than adults with IBD. These complicating factors can be mitigated by proactive TDM with preemptive dose escalation. Proactively optimizing therapy as patients age is important to maintain remission, prevent disease-related complications, optimize growth, and minimize corticosteroid exposure. Optimizing therapy is also of utmost importance in pediatrics to prolong treatment efficacy, prevent development of antidrug antibodies, and prevent loss of treatment options, as there are limited medications approved by the US Food and Drug Administration for this vulnerable population. This article reviews evidence for, and provides guidance on, proactive TDM in children and adolescents with IBD.

Keywords
Inflammatory bowel disease, pediatrics, therapeutic drug monitoring, dose optimization, advanced therapies

Inflammatory bowel disease (IBD) causes chronic inflammation and progressive damage to the intestines if not adequately treated. Early disease control is important to improve quality of life and prevent disease-related complications.[1-3] In children, disease control is complicated by several patient- and disease-related factors that can impact medication clearance.

Children tend to have more rapid drug clearance than adults at baseline.[4-6] Younger children and those who weigh less than 40 kg have even more rapid drug clearance than older and larger children.[7,8] Child growth and associated weight gain are nonlinear. Growth is fastest in infancy; growth slows but continues in middle childhood, and then increases again in adolescence. There are also changes in body composition as children go through puberty.[9,10] Additionally, IBD itself can cause growth delay owing to inflammatory cytokines, poor appetite, early satiety, and nutritional malabsorption.[11,12] As the disease improves with treatment, catch-up weight gain and growth should occur.[11,13,14] This is associated

Table 1. Target Drug Levels

Drug	Condition	Induction targets	Maintenance target
Infliximab	Uncomplicated IBD	2 wk, ≥29 μg/mL 6 wk, ≥18 μg/mL 14 wk, ≥7 μg/mL	>5 μg/mL
	Perianal disease	14 wk, >16 μg/mL	>16 μg/mL[a]
	VEO-IBD	2 wk, >23 μg/mL 6 wk, >16 μg/mL	>16 μg/mL
Adalimumab	Uncomplicated IBD	4 wk, ≥23 μg/mL 8 wk, ≥13 μg/mL	≥10 μg/mL
	Perianal disease	N/A	>15 μg/mL[a]
	VEO-IBD	N/A	N/A
Golimumab	Uncomplicated IBD	6 wk, >3.8 μg/mL	>2.4 μg/mL[a]
Vedolizumab	Uncomplicated IBD	2 wk, >23 μg/mL 6 wk, >22-28 μg/mL 14 wk, >17 μg/mL	>12 μg/mL
	VEO-IBD	N/A	N/A
Ustekinumab	Uncomplicated IBD	2 wk, >28-32 μg/mL 4 wk, >19 μg/mL 8 wk, >7 μg/mL	>4.5 μg/mL[a]

IBD, inflammatory bowel disease; N/A, not available; VEO-IBD, very early-onset IBD; wk, week.

[a]Nonhealing perianal disease may require higher levels.

with greatly accelerated metabolism, which can affect clearance of some medications.[6,15]

Children also tend to have more aggressive disease than adults independent of drug metabolism.[16,17] Aggressive disease commonly manifests in children as more extensive ulcerative colitis (UC) or, in Crohn's disease (CD), as more upper tract and small bowel involvement and greater propensity to develop perianal disease; in both diseases, there can also be increased extraintestinal manifestations and poor growth.[18,19] Greater disease activity itself is also associated with more rapid drug clearance, commonly requiring higher dosing of many advanced therapies.[8,20] Furthermore, children with CD commonly have greater tissue concentrations of cytokines such as tumor necrosis factor (TNF) and interleukin (IL)-6 than adults.[21,22] This increased TNF burden binds the anti-TNF medication and can act as a sink, resulting in less anti-TNF medication available and greater dosing requirement.[23,24]

For each of these reasons, the dosing of advanced therapies for pediatric IBD is not static and must be proactively adjusted to maintain long-term remission. This was demonstrated with high-quality evidence in the randomized PAILOT trial of children with CD who were advanced therapy–naive and responded to adalimumab induction.[25] They were then randomized to either proactive therapeutic drug monitoring (TDM) of adalimumab or usual care with reactive TDM as needed. Children in the proactive TDM group were more likely to have normalized fecal calprotectin (80% vs 30%; P<.001) and were more likely to be in corticosteroid-free clinical remission at 72 weeks compared with usual care (82% vs 48%; P=.002).

Early effective therapy and ongoing sustained effective therapy are both important to optimize a child's growth.[14,26] They are also important for preventing disease-related complications such as perianal, penetrating, and stricturing complications of CD, each of which are more common in children than in adults.[27-31]

Proactive TDM is also important for maintaining long-term persistence of treatment efficacy.[32] This is particularly important in children who will require treatment for decades, with only a limited number of medications approved. In a multicenter pediatric study, Ali and colleagues found that approximately 30% of pediatric IBD patients discontinued each advanced therapy, and 1 in 12 children with IBD had been treated with 3 or more advanced therapies before transferring to adult care.[33] In the current era, minimizing loss of treatment options is critically important because there are only 4 medications from 2 treatment classes approved by the US Food and Drug Administration (FDA) for treating pediatric IBD in the United States (infliximab, adalimumab, golimumab, and ustekinumab).

Table 2. Variations in Dosing Recommendations

Drug	Younger/smaller children	Older/larger children	Aggressive disease[a]
Infliximab	<40 kg: 200 mg/m² per dose	≥40 kg: 5 mg/kg per dose	10-20 mg/kg or higher
Adalimumab	CD 17 to <40 kg: Day 1: 80 mg Day 15: 40 mg Day 29: 20 mg every 2 weeks	CD ≥40 kg: Day 1: 160 mg Day 15: 80 mg Day 29: 40 mg every 2 weeks	Consider adding immunomodulator or using alternative advanced therapy
	UC 20 to <40 kg: Day 1: 80 mg Day 8: 40 mg Day 15: 40 mg Day 29: 40 mg every 2 weeks or 20 mg every 1 week	UC ≥40 kg: Day 1: 160 mg Day 8: 80 mg Day 15: 80 mg Day 29: 80 mg every 2 weeks or 40 mg every 1 week	
Golimumab	15 to <40 kg: 100 mg	≥40 kg: 200 mg	
Vedolizumab	<30 kg: 200 mg/m²	≥30 kg: 6-10 mg/kg up to 300 mg	Decrease dosing interval
Ustekinumab	Induction (IV) <40 kg: 250 mg/m² 40 to ≤55 kg: 260 mg	Induction (IV) 55 kg to ≤85 kg: 390 mg >85 kg: 520 mg	
	Maintenance (SC) 10-30 kg: 2.5 mg/kg every 8 weeks	Maintenance (SC) 90 mg every 8 weeks	Decrease dosing interval

CD, Crohn's disease; IV, intravenous; SC, subcutaneous; UC, ulcerative colitis.

[a]Aggressive disease includes severe colitis, extensive disease, faltering growth, and/or perianal disease.

Note: These doses are approximations. Proactive therapeutic drug monitoring should guide dose adjustments (Table 1).

In addition to the aforementioned clinical benefits of proactive TDM, studies indicate that proactive TDM may be cost-effective. Yao and colleagues used data from the PAILOT trial to model the cost difference comparing proactive TDM with usual care for pediatric patients treated with adalimumab.[34] The authors found that, over a 3-year period, ongoing proactive TDM led to a savings of more than $2000 compared with usual care with reactive TDM. Other studies have similarly demonstrated cost-effectiveness if not cost savings of proactive TDM.[35,36] This article reviews the evidence for TDM for advanced therapies and provides commonly recommended dosing for pediatric IBD in different scenarios.

Therapeutic Drug Monitoring in Clinical Practice

The most robust evidence for proactive TDM in IBD is for anti-TNF therapy. In pediatrics, infliximab and adalimumab have been the most studied as they were the only 2 FDA-approved options for pediatric IBD until October 2025. In a meta-analysis of patients with UC who experienced loss of response to anti-TNF therapy, 72% of those receiving infliximab were able to recapture clinical response with dose escalation, along with 52% of those receiving adalimumab, suggesting that many patients require higher-than-standard doses to achieve clinical benefit.[37] Real-world implementation of proactive monitoring in children has been found to both increase the odds of achieving sustained clinical remission at 52 weeks as well as decrease the risk of high titer antidrug antibodies.[38] It is important to note that treatment efficacy is dependent on drug exposure, not on the particular dose required to achieve adequate exposure. Treating children without ongoing TDM commonly results in subtherapeutic circulating drug levels and inadequate drug exposure. The benefit of TDM is conferred by ensuring consistent exposure to a sufficient amount of drug to maintain clinical efficacy. The evidence for TDM for each advanced therapy is summarized in Table 1. Commonly recommended dosing for pediatric IBD in different scenarios is provided in Table 2.

Infliximab

Historically recommended intravenous (IV) infliximab dosing of 5 mg/kg per dose has been found to be commonly inadequate to achieve target drug levels in pediatric IBD. Frymoyer and colleagues utilized a pharmacokinetic model to predict infliximab concentrations in pediatric

CD and found that only 41% of patients achieved even a subtherapeutic level of 3 μg/mL, with even lower levels found in patients with albumin less than 4 g/dL.[39] In pediatric CD, lower drug levels during induction have been associated with early failure and worse clinical and biochemical response. A study of proactive drug levels during infliximab induction in pediatric CD suggests that a week 2 level of at least 29 μg/mL and week 6 level of at least 18 μg/mL was needed to achieve adequate maintenance infusion levels.[40] A week 14 trough level of at least 7 μg/mL was found to be associated with concurrent clinical remission and reduced risk of antidrug antibodies, along with improved remission at week 54.[41] These induction and early maintenance level goals are in line with the recently published North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition (NASPGHAN) position paper on TDM in pediatric IBD.[8]

Subcutaneous (SC) infliximab has shown promising data for more stable drug exposure along with higher trough levels, with a large meta-analysis finding no significant difference in endoscopic remission at 54 weeks compared with IV infliximab.[42,43] Similar to the IV route, with SC administration, higher levels have been shown to portend better outcomes with clinical, biochemical, and deep remission.[44] Although pediatric studies in this regard are much smaller, they suggest that SC infliximab is associated with higher trough levels and strong treatment persistence.[45-47]

Adalimumab

Pediatric dosing recommendations for adalimumab are weight-based, dependent on classification of IBD.[48] As noted previously, the PAILOT trial demonstrated that pediatric CD patients with proactive TDM and subsequent dose intensification had improved fecal calprotectin levels and rates of clinical remission.[25] Additionally, Rinawi and colleagues found that proactive TDM with higher early adalimumab levels at weeks 4 and 8 were associated with more optimal clinical and biochemical outcomes at week 24.[49] Kennedy and colleagues determined that a week 14 trough level of at least 12 μg/mL was found to be associated with concurrent clinical remission and reduced risk of antidrug antibodies, along with improved remission at week 54.[41] The NASPGHAN position paper advocates for a target week 4 adalimumab level of 23 μg/mL and week 8 target of 13 μg/mL with maintenance goals of 10 μg/mL for optimal outcomes.[8]

Golimumab

Golimumab received FDA approval in October 2025 for moderate to severe UC in patients 2 years and older weighing more than 15 kg. The available evidence on TDM for golimumab is inconsistent. The GO-LEVEL phase 4 study assessing 39 adult patients with UC found that those who achieved clinical and biochemical remission at week 6 had higher drug levels with an optimal threshold of 3.8 μg/mL at week 6 and 2.4 μg/mL during maintenance.[50] In pediatrics, data on optimal drug levels are even more limited. The PURSUIT 2 study evaluated 69 advanced therapy–naive pediatric patients with UC and found drug trough concentrations at week 6 to be comparable with those of adults.[51] Overall, although pediatric-specific trials evaluating optimal trough levels are lacking, the pharmacokinetics of golimumab appears to be similar between children and adults. These target levels therefore may be appropriate for children.[52,53] However, some children require dose intensification of golimumab, so in the absence of pediatric-specific data, proactive monitoring is warranted in growing children with dose adjustment as needed to maintain adequate serum levels and disease remission.[54]

Vedolizumab

Although vedolizumab (Entyvio, Takeda) is approved by the FDA for the treatment of adults with moderate to severe CD and UC, vedolizumab is currently not approved for use in pediatrics. Despite this, it is frequently used off-label for the treatment of pediatric IBD given limited medication options and its favorable safety profile. In numerous pediatric studies, vedolizumab has been shown to effectively treat pediatric IBD. In the VEDOKIDS study, vedolizumab was shown to induce remission in 42% of pediatric patients with CD and 32% with UC.[7] In the KEPLER study, vedolizumab was shown to induce corticosteroid-free remission and maintain remission at 54 weeks in pediatric patients with moderate to severe UC.[55]

Higher serum concentration of vedolizumab is generally associated with better treatment outcomes for both UC and CD.[56] Target trough levels are derived from adult data, and smaller pediatric studies corroborate these findings.[7,57] Levels associated with treatment response are greater than 23 μg/mL at week 2 of induction, 22 to 28 μg/mL at week 6, greater than 17 μg/mL at week 14, and greater than 12 μg/mL prior to maintenance doses.[8]

Although traditionally administered intravenously, vedolizumab is increasingly used in a SC formulation. Studies of adult patients with IBD indicate that SC vedolizumab is as effective as IV vedolizumab.[58,59] However, there have been no pediatric-specific studies of SC vedolizumab to date, and both pharmacokinetics and weight-based dosing remain unclear, particularly for children less than 40 kg.

Ustekinumab

Ustekinumab is another medication that was used off-label for pediatric IBD until its recent approval by the FDA in April 2026 for treatment of children 2 years of age and older with moderately to severely active CD. There is currently no FDA approval for use in pediatric UC, although numerous pediatric studies have demonstrated that it is effective for the treatment of pediatric UC as well as CD. The REALITI study showed that ustekinumab induced clinical and corticosteroid-free remission in a subset of pediatric patients with CD, often in patients who had already used at least 1 other advanced therapy.[60] Cohen and colleagues showed that ustekinumab therapy also induced corticosteroid-free remission in a subset of pediatric patients with UC and unclassified IBD.[61]

Limited pediatric evidence suggests that higher ustekinumab serum levels are associated with greater treatment efficacy, although the data are mixed and target serum levels are not certain. These studies are limited by small sample sizes and skewed populations with more aggressive phenotypes given this medication has traditionally been used in patients who have failed other advanced therapies. The study by Cohen and colleagues of ustekinumab use in pediatric UC showed no difference in serum ustekinumab levels between those who achieved remission and those with active disease. Interestingly, in this study, a subset with active disease underwent dose escalation, and most in that subgroup had subsequent better control of disease, suggesting that higher serum levels have a positive impact on disease control.[61] Straatmijer and colleagues showed that, in a larger group of pediatric patients with CD, those who achieved biochemical remission had higher serum ustekinumab levels than those who did not. However, in this study, there was no difference in levels between those who achieved clinical remission and those who did not.[62]

Ultimately, adult data inform current pediatric practice, with proactive TDM shown to be associated with increased drug persistence and better outcomes.[63] One study suggests a week 2 target level of greater than 28 to 32 μg/mL, a week 4 target level of greater than 19 μg/mL, and a week 8 target level of greater than 7 μg/mL.[64] A maintenance trough level greater than 4.5 μg/mL is associated with mucosal healing in adult data, which is in line with the recently published NASPGHAN position paper on TDM in pediatric IBD.[8,65]

Interleukin-23 Inhibitors

Risankizumab (Skyrizi, AbbVie), mirikizumab (Omvoh, Lilly), and guselkumab (Tremfya, Janssen) are approved for the treatment of moderate to severe CD and UC in adult patients. No IL-23 inhibitors are approved for use in pediatric IBD, although they are increasingly used off-label. Limited data suggest that risankizumab successfully treats pediatric IBD. There are many reports of successful risankizumab use for pediatric IBD in patients who have failed to respond to at least 1 advanced therapy, further suggesting efficacy.[66] However, at this time, there are no large peer-reviewed studies in pediatrics to date.

There is currently scant evidence to suggest a relationship between IL-23 inhibitor levels and disease outcomes.[67,68] Risankizumab and guselkumab assays are commercially available, although without evidence to inform target serum levels, the clinical value of TDM is unclear at this time.[69]

Proactive Dose Escalation

Instead of waiting for inadequate levels with proactive TDM or development of worsening disease and reactive TDM, certain pediatric populations benefit from initiating high-dose therapy from the start or preemptive dose escalation. Inadequate dosing carries consequential morbidity with the risk of antidrug antibodies, which can render an effective therapy ineffective. The REFINE study was a multicenter prospective cohort evaluating pharmacokinetics where clinicians were blinded to the levels.[70] This study illustrated that induction doses of infliximab of at least 7.5 mg/kg per dose significantly reduced its immunogenicity risk compared with starting with lower doses.

Younger and smaller children have consistently demonstrated a need for higher dosing of most advanced therapies to achieve adequate levels and disease control. Zhao and colleagues conducted a pharmacokinetics study, which revealed that patients 10 years of age and younger have higher infliximab clearance compared with older pediatric patients and adults.[6] This is possibly secondary to the nonlinear relationship between weight and body surface area (BSA), with evidence suggesting that patients below 40 kg have more optimal infliximab doses with 200 mg/m² dosing compared with weight-based dosing.[71] For patients with very early-onset IBD, those with disease onset before 6 years, optimal infliximab induction levels have been found to be a week 2 level greater than 23 μg/mL and week 6 level greater than 16 μg/mL.[8] The VEDOKIDS study showed that smaller patients, less than 30 kg, receiving vedolizumab also benefit from dose escalation with dosing of 200 mg/m² or 10 mg/kg, with these doses more likely to achieve serum drug levels that correlated with corticosteroid-free remission at 14 weeks.[7] Similarly, standard dosing of ustekinumab for patients less than 40 kg resulted in lower serum concentrations, so BSA-based dosing of 250 mg/m² is being utilized for

a phase 3 pediatric CD clinical trial based on pharmacokinetic data.[72]

Pediatric patients with more severe disease burden have also demonstrated the need for higher anti-TNF dosing. Higher serum inflammatory markers in pediatric IBD are associated with a greater likelihood of infliximab nonresponse.[73] Low serum albumin (<4 g/dL) can lead to increased drug clearance secondary to protein-losing enteropathy and has been established to be associated with lower drug levels.[39,74] Furthermore, patients with corticosteroid-refractory acute severe UC have higher infliximab clearance rates associated with increased risk of treatment failure.[75] These patients often benefit from 10 mg/kg infliximab doses.

Perianal CD commonly requires higher drug levels for better response. Pediatric CD patients receiving anti-TNF therapy were found to have faster healing of fistulizing disease if they underwent TDM.[76] In a cross-sectional study of 117 adults with perianal CD treated with infliximab, those who achieved fistula healing with absence of drainage had higher median drug levels (15.8 vs 4.4 μg/mL).[77] In a prospective inception cohort of children with CD, El-Matary and colleagues described 85 children with perianal fistula, among whom 27 had infliximab levels available at the end of infliximab induction.[78] The authors found that a higher induction infliximab level was associated with improved fistula healing by 24 weeks (12.7 vs 5.4 μg/mL). In a retrospective cohort of pediatric patients with perianal CD treated with 5 mg/kg per dose infliximab, 42% of those with a clinical response required dose escalation within the first year of treatment.[79] There are less robust data for optimal adalimumab levels for perianal CD. A retrospective cross-sectional study of 35 patients found that higher levels were needed to resolve perianal fistula drainage with even higher levels required to achieve closure (14.8 vs 5.7 μg/mL).[80] Papamichael and colleagues conducted a retrospective multicenter study of adalimumab treatment of perianal disease in adults with CD.[81] In this study, the authors defined fistula healing as total absence of fluid in the tracts on imaging and/or physician global assessment. They found that a maintenance adalimumab level of at least 14.3 μg/mL was associated with 63% healing. Thus, the target trough levels for perianal disease are greater than 16 μg/mL for infliximab and greater than 15 μg/mL for adalimumab.[8]

Dose escalation should also be considered in patients with HLA-DQA1*05 carriage.[82] In a randomized trial of pediatric patients with CD receiving anti-TNF therapy, HLA-DQA1*05–positive patients on monotherapy had the highest rates of treatment failure in addition to immunogenicity with risks mitigated by adjunctive methotrexate.[83]

Additionally, when considering techniques to mitigate risk of inadequate drug levels, dual therapy with an adjunctive immunomodulator can be contemplated. In the COMBINE trial, pediatric CD patients receiving methotrexate adjunctive to adalimumab had less treatment failure than those receiving anti-TNF monotherapy, although this was not replicated for infliximab in this study.[84] Dual therapy can be a useful technique for promoting advanced therapy longevity; however, given the risk of added side effects and immunosuppression, proactive dose escalation with proactive TDM to ensure adequate levels and diminish immunogenicity is likely the safer option.

Of note, despite ample evidence that TDM results in improved outcomes for pediatric patients with IBD, insurance denial of appropriately prescribed drugs or doses needed to achieve adequate drug levels is pervasive. Constant and colleagues showed that numerous barriers to prescribing an intended drug and/or dose arise from medically inappropriate insurance mandates, including prior authorization requirements and dose restrictions.[85] These barriers and restrictions against evidence-based care lead to undertreatment and result in 60% of patients experiencing harm, including decrease in quality of life and increases in blood transfusion, hospitalization, and need for surgery.

Conclusion

Children with IBD present unique pharmacokinetic- and disease-related challenges that necessitate proactive TDM with an individualized approach to dosing targets. Universal implementation of TDM can result in improved clinical outcomes with prevention of disease-related complications and improved advanced therapy longevity with lower risk of development of antidrug antibodies. This is of utmost importance in this vulnerable population that has limited approved medical therapies, more aggressive disease, and longer duration of disease compared with adults. Preemptive dose escalation should be utilized in high-risk populations, including younger and smaller children, those with extensive or severe disease, hypoalbuminemia, perianal complications, and possibly HLA-DQA1*05 carriage. This evidence is robust for infliximab and adalimumab in pediatrics with mounting data for ustekinumab and vedolizumab guiding pediatric practice. Prospective pediatric trials are needed to validate target drug levels, refine dosing strategies, and elucidate more definitive practice for emerging therapies such as IL-23 inhibitors. The recently published NASPGHAN position paper on TDM provides a framework for implementing this into clinical practice in all settings where children and adolescents with IBD are cared for.

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