

# Assuring Quality for Non-hospital–based Biologic Infusions in Pediatric Inflammatory Bowel Disease: A Clinical Report From the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition

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## ABSTRACT

The primary aim of this Clinical Report by the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition is to provide formal guidance to pediatric gastroenterologists and clinicians, health systems, and insurance payers regarding home- and office-based infusions for biologic therapies in pediatric inflammatory bowel disease. Patients in North America are increasingly denied coverage by payers based on “place of service” codes at hospital-based infusion units where the treating clinicians primarily provide care. A task force with topic expertise generated 8 best practice recommendations to ensure quality of care for pediatric patients with inflammatory bowel disease receiving non-hospital–based biologic infusions. Pragmatic considerations discussed in this report include patient safety, pediatric-trained nurse availability, care coordination, patient-centeredness, shared liability, administrative support, clinical governance, and costs of care.

**Key Words:** biologics, Crohn disease, home infusions, home-based infusions, infliximab, ulcerative colitis, vedolizumab

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## 1. SCOPE AND PURPOSE

### 1.1. Introduction and Aims

Inflammatory bowel disease (IBD), which encompasses both Crohn disease (CD) and ulcerative colitis (UC), is a chronic condition with increasing global incidence during the childhood and adolescent years (1). Approximately one-quarter of new diagnoses are in patients less than 20 years of age, and pediatric onset of disease has been associated with increased disease-related comorbidities and costs of care (2,3). Evidence-based use of biologic therapies in pediatric IBD has improved health outcomes in this vulnerable patient population. While effective, the use of infliximab and vedolizumab—the 2 primary biologic infusion therapies currently used in pediatric IBD—requires proactive monitoring and coordination of care to ensure optimal safety and quality of care.

In developing this clinical report, the task force made careful consideration of the differences in physician practices depending on numerous variables (eg, academic or private practice, geographic

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The NASPGHAN practice guidelines are evidence-based decision-making tools for managing health conditions. Practice Guidelines include Clinical Practice Guidelines (CPGs), clinical reports, technical reports, and position statements. They are authorized by the NASPGHAN Executive Council, peer reviewed, and periodically updated.

They are not to be construed as standards of care and should not be construed as establishing a legal standard of care or as encouraging, advocating, requiring, or discouraging any particular treatment. All decisions regarding the care of a patient should be made by the health care team, patient, and family in consideration of all aspects of the individual patient’s specific medical circumstances.

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location, patient population, clinical support staff, access to care and regionalization, IBD-specific referral centers, etc). Although home- or office-based infusions may provide high-quality care for many practices (4), in-home service agencies and office-based infusion sites are often not affiliated with the treating physician's health system or practice group, which can become a source of fragmentation of care leading to worse quality. In addition, there is an absence of regulations regarding infusion practices. We acknowledge that home- or office-based infusions can be patient-centered, convenient for patients and families, and sometimes preferred if pediatric-specific quality measures are in place and implemented reliably.

The primary aim of this clinical report is to provide formal guidance by the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN) to pediatric gastroenterologists and clinicians, health systems, and insurance payers regarding home- and office-based infusions for biologic therapies in pediatric IBD. The target audience of this clinical report is pediatric gastroenterologists, nurse practitioners, and care team members treating pediatric IBD patients. These considerations were developed specifically for children affected by IBD living in North America, particularly in the United States, where hospital-based infusions are increasingly denied coverage by payers based on "place of service" codes (5), authorizing infusions only at home- or office-based locations (eg, site-of-care shifts).

## 2. DEVELOPMENT OF THE CLINICAL REPORT

### 2.1. Selection of Topics and Task-force Members

In 2016, the Clinical Care & Quality (CCQ) Committee of NASPGHAN determined the need for formal clinical practice guidance to ensure optimal safety and coordination for children affected by IBD who are receiving biologic therapies outside of the traditional hospital setting. Key topics of discussion were developed in committee meetings and with consultation from select members of the IBD Committee. Based on recommendations from both committees, a list of key opinion leaders in the field of pediatric IBD was generated to identify those with clinical expertise and reputation in the field. After a systematic review of the available literature, the final task force selection process was based on the results of a web-based survey to determine topic expertise and real-world clinical experience providing and managing home- or office-based biologic infusions for pediatric IBD. All members on the task force developed the proposal drafts and timeline with NASPGHAN Council's approval in January 2017.

### 2.2. Organization of Task Force Into Working Groups

Once the task force members (ie, authors of this clinical report) were finalized, 2 separate working groups were formed to focus on patient- and provider-centered considerations. Each of the 2 working groups independently generated clinical case scenarios that informed the overall task force's determination of the key considerations to be included in this clinical report. The first working group (E.B., L.S., R.S., S.K., J.M., A.G., and K.P.) generated 4 patient care considerations for home- or office-based infusions: patient safety, pediatric nurse availability, patient and family quality of life, and establishment of a standard of care. The second working group (E.B., J.P., S.S., G.W., D.D., E.H., and K.P.) generated 4 logistical considerations for home- or office-based infusions: liability, administrative support and policy, proactive care and clinical governance, and cost and remuneration.

## 3. PATIENT CARE CONSIDERATIONS

### 3.1. Ensuring Patient Safety

Recommendation 1: Home- or office-based infusions should ensure safe administration of the biologic infusion, provide reliable execution of infusion-related orders (eg, laboratories for therapeutic drug monitoring, dose optimization protocols, etc), and be equipped to recognize and respond to potential complications.

Patient safety has been identified as a primary concern for home- or office-based biologic infusions. Biological therapies for IBD treatment are complex protein–based compounds and their molecular structure is larger and more complex compared to standard pharmacological small molecule preparations. Infusion reactions associated with infliximab and vedolizumab can range from mild reactions such as fever and chills, dyspnea, pruritus, or urticaria (in approximately 5%–10%), to severe reactions including anaphylaxis, convulsions, and hypotension (<1%) (6,7), although recent data in children receiving infliximab suggest extremely low risk of anaphylaxis during administration (8). Given infusion-associated risk (9), children need special consideration. In particular, children who have challenging venous access and those with very early onset IBD (VEO-IBD) as defined by the Paris modification of the Montreal Classification may be at increased risk of more severe infusion reactions (10), and home infusions may not be appropriate for these younger patients.

In the event of an urgent or emergent reaction during home- or office-based infusions, the in-home services agency (IHSA) nurse needs to be able to contact the appropriate ordering medical team member expeditiously by phone or pager to review/clarify specific concerns or needs to have an established clear policy on how to proceed with managing the reaction. Examples of such a policy include orders for appropriate medications to administer and laboratories to draw such as a complete blood count, liver enzymes, pancreatic enzymes, and lactate dehydrogenase if requested by the treating provider. We identified the lack or inconsistency of on-call coverage by the primary medical team when home- or office-based infusions occur as a significant barrier to safely initiating or continuing home- or office-based infusion programs. Difficulty in reaching a knowledgeable team member is a breach in reliable care and represents serious patient risk. We recommend establishing clear communication pathways for urgent questions by the IHSA nurse whenever necessary.

While the ability to reach a medical team member is required, we also acknowledge the real-world logistical challenge of having a covering team member be knowledgeable about each patient's unique case and home- or office-based infusion protocol. Clinical practices are different, often depending on geography, patient population, and practice model. These differences may help or hinder establishing this ideal clinical coverage. Regardless, clear practice-specific protocols are needed for emergency care, and the patient's family should be educated to call the provider in advance of the scheduled infusion if the patient is having a fever or feeling ill to receive individualized patient advice for the upcoming infusion, regardless of the location (eg, home-, office-, or hospital-based). A parent or legal guardian of the pediatric patient should be present during the home- or office-based infusion.

In addition to administering the biologic infusion, executing all other infusion-related orders is an important safety consideration. Implementing unique home infusion protocols is linked to treatment efficacy. The IHSA nurse should have pediatric-specific

skillsets to clinically assess patients before and during the infusion, particularly in children with other co-morbidities or chronic conditions. We recommend that infusion order sets be well-defined with clear nursing guidelines. Without clarity, the infusion should be postponed until details can be clarified with the physician or team member. Such clarification of orders often relates to dose optimization or escalation and therapeutic drug monitoring laboratories (11). The individualization of biologic dosing should be executed in a safe and reliable manner regardless of the site of infusion.

Finally, the decision for when a pediatric patient should begin receiving home- or office-based infusions is patient-specific and driven by safety and quality considerations. We suggest that treating physicians work with each patient and family to determine the optimal location (hospital-, home-, or office-based) of infusions based on different, patient- and provider-specific considerations. If home- or office-based infusions are payer-mandated, the treating physician should consider patient safety as a top priority. Additionally, in keeping with the National Home Infusion Association's Standards on Ethical Practice (12), we support the patients' and families' decision-making process regarding the preferred site of care for infusions. Pediatric gastroenterology practices should develop a formal education program about home- or office-based infusion therapies to bring consistency and establish consensus within the practice. Whenever possible, we recommend developing institution-specific screening criteria to determine when a patient may be eligible for home- or office-based infusions (eg, absence of prior infusion reactions, achieving target drug trough levels while in sustained clinical remission, demonstrating compliance, etc). The task force emphasizes that these safety considerations apply to all sites of administration of biologics including the home-, office-, and hospital-based settings.

### 3.2. Pediatric Nurse Availability

Recommendation 2: Pediatric home- or office-based infusions, particularly for patients 12 years and younger, should be staffed by a pediatric nurse professional with Pediatric Advanced Life Support (PALS) certification and clinical experience with pediatric patients.

Pediatric nurse availability is an important consideration when providing home- or office-based biologic infusions in children 12 years and younger, and we strongly recommend that pediatric-trained nurses staff the home- or office-based infusions for this age group. Pediatric nurses have experience in assessing and interacting with children at different developmental stages. They should also be experienced in working with families caring for chronically ill children. Nurses administering the infusions in children 12 years and younger should be certified in PALS and equipped to manage a medical emergency.

Establishing intravenous access and performing venipuncture in young patients is an important skill and should be considered a necessary qualification criterion for a nurse professional caring for children receiving home- or office-based infusion therapies through an IHSA. Regular difficulty with intravenous access or venipuncture may offset any convenience or quality-of-life gained from home- or office-based infusions from the perspective of the family and pediatric patient, and delay of treatment based on inability to establish access can have deleterious effects on clinical and psychological outcome. Of note, 1 limitation of home- or office-based infusions is the lack of access to

a vascular access team or specialized instruments such as ultrasound to help establish intravenous access in difficult cases. A history of previous or current difficulty in obtaining vascular access is an important consideration for infusions to remain hospital-based.

### 3.3. Establishing a Standard of Care

Recommendation 3: Evidence-based standard of care for biologic therapy maximizing effectiveness and treatment sustainability should be established before initiating home or office-based infusions.

In the context of known practice variability between treating physicians using biologic therapies (13,14), we highlight the importance of evidence-based, "best practice" care for biologic therapies (15,16), regardless of where patients receive their infusions. We identified these criteria for establishing a standard of care for home- or office-based biologic infusions in keeping with best practices:

1. Demonstrated safety of maintenance infusions after induction doses. We do not recommend initiating induction doses of biologic therapies at the patient's home.
2. Scheduled (not episodic) maintenance of infusions as ordered by the treating physician.
3. Scheduling flexibility to quickly and easily change drug dosing and interval when clinically warranted.
4. Care coordination of communication and laboratory results.
5. Protection of patients and families from increased out-of-pocket costs (compared to hospital-based infusions).
6. Requirement for regular follow-up visits, as determined by the provider overseeing IBD care.

Scheduled maintenance infusions are important to ensure optimal drug sustainability. Patients who receive home infusions will require extensive education that episodic biologic therapy will increase the risk of premature drug failure and adverse reactions through early drug tolerance and autoantibody formation (17,18). We support adherence to an agreed-upon, scheduled therapy plan and follow-up visit plan as recommended by the treating pediatric gastroenterologist. Failure to meet this criterion by either the patient or IHSA is grounds for non-initiation or termination of home- or office-based infusions. Scheduling flexibility (eg, providing the next scheduled infusion earlier) is an important requirement to personalize therapy plans for individual patients needing dose optimization. Specifically, clinical symptoms consistent with disease exacerbation (eg, symptom reporting and disease activity indices) or other objective parameters (eg, elevations in calprotectin or C-reactive protein) may warrant efficient scheduling of an expedited infusion before that previously scheduled; the IHSA must be able to provide reasonable flexibility to allow for such individualized dosing and interval changes when clinically necessary (11). If this cannot be provided, patients/providers must be allowed flexibility to schedule an expedited infusion at a hospital-based infusion unit in order to provide timely, appropriate care (Table 1).

Care coordination of communication (nursing documentation) and laboratory results are necessary for proactive IBD care. High-value care requires bidirectional communication between the

TABLE 1. Best practice recommendations

Recommendation 1	Home- or office-based infusions should ensure safe administration of the biologic infusion, provide reliable execution of infusion-related orders (eg, laboratories for therapeutic drug monitoring, dose optimization protocols, etc), and be equipped to recognize and respond to potential complications.
Recommendation 2	Pediatric home- or office-based infusions, particularly for patients 12 years and younger, should be staffed by a pediatric nurse professional with PALS certification and clinical experience with pediatric patients.
Recommendation 3	Evidence-based standard of care for biologic therapy maximizing effectiveness and treatment sustainability should be established before initiating home- or office-based infusions.
Recommendation 4	Home- or office-based infusion pathways that decrease opportunity loss for patients and families and deliver high-quality, patient-centered care should be supported and reproduced.
Recommendation 5	Pediatric gastroenterologists should ensure appropriate shared liability with IHSAs to deliver high-quality care in home-based infusions for children by executing pragmatic steps as outlined (a–h) in this report.
Recommendation 6	A more equitable division of labor should be established to offset increased administrative burden placed on the pediatric gastroenterologist and medical team to effectively facilitate and maintain home- or office-based infusions, especially when driven by payer-mandated policies.
Recommendation 7	Clinical governance should be discussed and agreed upon with the patient and family before beginning home- or office-based infusions. Among patients receiving home- or office-based infusions, unreliable follow-up care with the provider as scheduled is grounds for discontinuation of home- or office-based biologic therapy.
Recommendation 8	A proper appeals process should be in place to prevent cost transference from payer to patient in payer-mandated decisions for home- or office-based infusions.

IHSA = in-home services agency; PALS = Pediatric Advanced Life Support.

patient and the treating physician or medical team regarding patient-reported outcomes, which are used to assess disease activity scores at or around the time of the infusion. We recommend establishing clear communication pathways between the patients/families, IHSA and their staff, and the medical team. A process of standardization of laboratory results being consistently and expeditiously forwarded to the treating physician and medical team for review is considered imperative for effective and reliable care coordination.

Finally, protection of patients and families from higher, unnecessary out-of-pocket costs should be considered. The push for home- or office-based infusions may be driven by insurance companies authorizing a site of care shift from hospital-based infusions to home- or office-based infusions based on the place of service (4). Such payer-mandated trends have diverted the location of authorized service away from the health system where the medical team is primarily located. Home- or office-based infusions may result in higher out-of-pocket contribution for families affected by IBD. If a payer-mandated site-of-care shift resulting in home- or office-based infusions increases out-of-pocket costs compared to hospital-based infusions, we recommend initiating a separate appeals process with expeditious resolution of the issue to offset any effects on clinical care.

### 3.4. Minimizing Opportunity Loss

Recommendation 4: Home- or office-based infusion pathways that decrease opportunity loss for patients and families and deliver high-quality, patient-centered care should be supported and reproduced.

We support home- or office-based infusion pathways already established at various institutions and pediatric gastroenterology practices delivering high-quality, patient-centered care. Such models provide the patients and families scheduling flexibility, often leveraging non-business hours. Weeknights and weekend

infusions—if available—decrease opportunity loss by minimizing or eliminating missed work for parents and school for patients (19). Children affected by IBD are already known to have increased school absences due to disease-related illness and medical care visits (20). Other indirect costs may be avoidable if effective home- or office-based infusion options are available, including costs of food, lodging, transportation, and child care. Minimizing indirect costs may be particularly impactful for patients and families traveling long distances to receive infusions or patients with poor access to health care infrastructure (21).

Although more research is needed, patients receiving effective home- or office-based infusions report comfort and a pleasant experience receiving therapy at home (22). Children receiving home- or office-based infusions may experience less anxiety in the home setting than in health care facilities. Alternatively, special considerations unique to the pediatric patient may be needed, particularly in children with high anxiety levels, psychiatric illnesses, and behavioral issues that may mandate hospital-based infusion administration.

## 4. LOGISTICAL CONSIDERATIONS

### 4.1. Liability

Recommendation 5: Pediatric gastroenterologists should ensure appropriate shared liability with IHSAs to deliver high-quality care in home-based infusions for children by executing pragmatic steps as outlined below (a–h).

Liability is defined as being responsible for some action according to law. Regardless of the site of infusion, it is the responsibility of the physician prescribing a biologic therapy to discuss risks and benefits of therapy with the patient and family before the first drug administration and to *prescribe* these biologics appropriately. The hospital-based infusion center or IHSA holds responsibility to *deliver* these medications appropriately (23).

The individual state department of health sets the minimum health and safety standards for IHSA licensure to provide home care. Depending on the range of services to be provided by an IHSA, state licensure may not be required. Although accreditation (by satisfying licensing and other regulatory requirements imposed by state pharmacy boards) is voluntary, most commercial insurers require IHSAs to be accredited to serve their insured patients. Given this, we support that insurance companies allow input from pediatric gastroenterologists and families if they have safety concerns about poorly performing IHSAs. Regardless of formal guidance by the state (eg, PALS certified RN requirement), NASPGHAN supports each of the individual considerations as outlined in this clinical report. In clinical practice, pediatric gastroenterologists should carefully review all orders, particularly order sets by the IHSA, and refuse signing orders that unduly transfer risk from IHSA to the physician.

Furthermore, we recommend outlining a clear plan of action for safe access to an emergency medical services (EMS) team as determined by the prescribing provider and IHSA—especially in areas where health care access may be limited. Of note, some infusion services may consider home locations to be safe if they are within 30 minutes of EMS access and the treating physician may need to determine if this is acceptable on a case-by-case basis.

We have developed and recommend the following pragmatic steps to ensure appropriate shared liability for the prescribing pediatric gastroenterologist working with IHSAs:

1. Document discussion with the patient and family about the indication, risks, and adverse event management related to the biologic therapy. (For example, “Discussed with the patient and family the indication of X therapy for moderate-to-severe Crohn disease, the adverse events including but not limited to allergic reactions, infection, skin lesions, immunosuppression and the monitoring plan. All questions related to the biologic therapy have been answered. Patient and family expressed understanding and agree to proceed with home biologic therapy.”)
2. Refer the patient to an accredited, licensed IHSA based on patient’s insurance coverage. If no accredited, licensed IHSA for the pediatric patient exists, this is grounds for not initiating home- or office-based infusions, and an appeals process may be necessary to continue hospital-based infusions.
3. Use an infusion protocol, either prescribed by the treating physician or provided by the IHSA and reviewed/approved by the provider.
4. Use an infusion reaction protocol with clear directives on recognition of signs/symptoms of reactions and administration of reaction medications and use of EMS or parent transport to an emergency room.
5. Maintain accurate documentation and communication of therapy type, dose, and frequency.
6. Provide a reliable communication mechanism for the IHSA to notify provider of changes or infusion-related events (See 3.3 Establishing a Standard of Care).
7. Regularly reviewing ongoing IHSA performance with regard to delivery of services, accurate laboratory ordering and turn-around time, safety and quality concerns and timely redressal of these issues.
8. Switch to another IHSA if the performance reliability is unsatisfactory. Since IHSAs are often contracted with specific payers, we acknowledge that changing IHSAs may be difficult.

## 4.2. Administrative Support and Policy

**Recommendation 6:** A more equitable division of labor should be established to offset increased administrative burden placed on the pediatric gastroenterologist and medical team to effectively facilitate and maintain home- or office-based infusions, especially when driven by payer-mandated policies.

Among some of the most time-consuming and difficult tasks associated with providing biologic therapies like infliximab and vedolizumab is the administrative support necessary for patients to receive home infusions. Issues include patient enrollment in different insurance plans or changes made by the insurance company including changes in benefits. Navigating the insurance pre-approval process to initiate biologic therapy or to request home- or office-based infusions may take days to weeks. Recently, many payers’ policies have changed, and patients may be asked to participate in some of the insurance navigation as well—a task which can be daunting and frustrating for families attempting to obtain necessary treatment for an ill child.

A variety of practice patterns exist across the country that dictate how the prior authorization process and appeals are completed and may include the physician, an administrative assistant, nurse or nurse practitioner, social worker, medical assistant or centralized approval structures. Reliance on IBD-inexperienced, non-medical providers to navigate the prior authorization process is problematic if medical knowledge is required. Well-supported, knowledgeable administrative teams working together are necessary to ensure timely and accurate initiation of biologic therapy in the home setting.

Although outside the scope of this clinical report, we highlight the increasing administrative burden (not specific to pediatric gastroenterology) on health systems and health care professionals as a result of payer-mandated policies for coverage of rendered services, such as biologic infusions. We acknowledge the urgency in developing fair and more equitable policies at state and federal levels aimed to redistribute the current disparate responsibilities levying the time and energy of physicians, medical staff, and patients and their families.

For home- or office-based infusions, specific policy guidance is required regarding whether the provider or the IHSA is responsible for obtaining prior authorization for home- or office-based biologic therapy. Currently, time and burden for this process are placed on the provider and the medical team. While it is the provider’s responsibility to advocate for the patient to receive the best care, IHSAs financially benefit from the patient referrals. Providers and the medical team render time and energy necessary for patients to receive biologics at home, but the prevailing business model diverts appropriate remuneration needed to support the administrative work at the physician’s institution and clinical practices (see Section 4.4 Cost and Remuneration). Furthermore, the increasing administrative burden falls on the provider and medical staff while fragmentation of care amplifies the administrative work required to facilitate care coordination between 3 separate entities: provider, IHSA and patient/families (see Sections 3.3 Establishing a Standard of Care and 4.3 Proactive Care and Clinical Governance).

### 4.3. Proactive Care and Clinical Governance

Recommendation 7: Clinical governance should be discussed and agreed upon with the patient and family before beginning home- or office-based infusions. Among patients receiving home- or office-based infusions, unreliable follow-up care with the provider as scheduled is grounds for discontinuation of home- or office-based biologic therapy.

Proactive IBD care involves longitudinal disease activity monitoring and achievement of corticosteroid-free remission with the goal of endoscopic and histologic healing (24). Proactive care is preferred rather than a reactive approach to care whereby treatment adjustments are made after overt disease exacerbation, often leading to rescue corticosteroid use and potentially worse health outcomes (25).

In pediatric IBD, sustainability of long-term remission is the goal through proper surveillance (26) (eg, minimum of bi-annual visits) in even asymptomatic patients (27). We recommend prioritizing patient and family education to ensure that proactive IBD care is a shared goal. Some centers of excellence have implemented a patient-provider contract to help execute this shared goal model. If disruption of recommended care occurs, this should be grounds for discontinuation of order renewal for home- or office-based biologic therapies and infusion-related orders, wherein patient should be switched back to hospital-based biologic infusions until the situation is resolved to the satisfaction of the medical team and meets the standard of care.

Clinical governance should be discussed and agreed upon with the patient and family affected by IBD before initiating home- or office-based infusions. Clearly established clinical processes (28) for the care team would decrease the likelihood of fragmented care for patients receiving home- or office-based infusions. Such organized governance plans are particularly important if decision-making may unexpectedly fall on medical team members after normal business hours (eg, on-call clinical fellows and attending physicians). Clear, bidirectional communication pathways are needed between the patient and the pediatric gastroenterologist to ensure seamless administration of home- or office-based infusions and appropriate follow-up visits to the provider.

### 4.4. Cost and Remuneration

Recommendation 8: A proper appeals process should be in place to prevent cost transference from payer to patient in payer-mandated decisions for home- or office-based infusions.

Direct costs associated with infliximab or vedolizumab infusions are disproportionately higher than any other therapies in IBD. Evidence suggests that utilization of biologics is outpacing the use of other pharmaceutical options. Aggregate pharmacy related costs for IBD care are driven by biologic use and account for the single largest driver for the cost of IBD care (3). Considering the multiple factors for increasing use of biologics, patients and families may be more vulnerable to out-of-pocket costs when biologics are mainstay therapy. This is particularly applicable if home- or office-based infusions have higher deductibles compared to office- or hospital-based infusions. Shifting costs

of care from the payer to patients is not acceptable, particularly if driven by payer-mandated decisions. Cost transference from payer to patient may be compounded by increasing selection of high deductible health plans. Families affected by IBD need transparency of patient-responsible costs if biologics are to be infused at various locations (see Section 3.4 Minimizing Opportunity Loss).

Remuneration of services rendered by the pediatric gastroenterologist or medical team is an important service fee that is often not reimbursed when patients receive home- or office-based infusions. Facility charges are considered for each hospital-based infusion, allowing profit margin to the administering health care facility. For home- or office-based infusions, care coordination efforts (see Section 4.2 Administrative Support and Policy) by the physician or medical staff are not automatically captured as a rendered service. We recommend pediatric gastroenterologists and staff use the Current Procedural Terminology (CPT) code 99374 “Care for Oversight Services” (supervision of patient under care of an IHSA) which generates 1.1 RVUs for care coordination efforts from 15 to 29 minutes such as administrative work required to ensure proper drug and review of laboratory results and orders with the IHSA. No evaluation and management (E/M) code is required to bill this CPT code. However, effective use of this CPT codes may vary based on payer to health system contracting, level of needed documentation, and method of physician billing based on practice type.

## CONCLUSIONS

The task force acknowledges that clinical practice variation and differences between individual patients and families prevent uniform endorsement of 1 location of service for pediatric biologic infusions. Fragmentation and poor quality of care can ensue in any setting. However, special considerations are needed to ensure high-quality home- or office-based infusions. These considerations as outlined in this clinical report represent challenges as well as opportunities for improved patient-centeredness. For treating physicians and care teams, ensuring these considerations are implemented could reduce logistical barriers in providing high-quality care.

In an effort to ensure high-quality care, pediatric gastroenterologists and medical teams are currently enduring substantial administrative burden without appropriate remuneration for services rendered. Existing mechanisms for equitable compensations are inadequate. Transference of administrative burden from payer to providers is not specific to pediatric gastroenterology, and ongoing advocacy and strategic policy efforts are needed by NASPGHAN and other affected organizations, including Crohn’s & Colitis Foundation, American Gastroenterological Association, and American College of Gastroenterology.

While outside the scope of this clinical report, the task force acknowledges the growing acceptance and use of biosimilars in the treatment of IBD. The task force recommends that ordering physicians are notified if there is any change to the physician’s order, especially as pertains to automatic substitution of the originator biologic to the biosimilar.

Finally, the task force highlights the current challenge of prioritizing patient and family preferences for the location of infusion (eg, hospital-, office-, or home- or office-based), which are often not considered in payer-mandated site-of-care decisions. Although the scope of this clinical report specifically applies to home- or office-based infusions, the considerations outlined here are applicable to hospital-based and free-standing centers providing infusions where the treating gastroenterologist does not have direct affiliation.

## REFERENCES

1. Benchimol EI, Fortinsky KJ, Gozdyra P, et al. Epidemiology of pediatric inflammatory bowel disease: a systematic review of international trends. *Inflamm Bowel Dis* 2011;17:423–39.
2. Pigneur B, Seksik P, Viola S, et al. Natural history of Crohn's disease: comparison between childhood- and adult-onset disease. *Inflamm Bowel Dis* 2010;16:953–61.
3. Park KT, Colletti RB, Rubin DT, et al. Health insurance paid costs and drivers of costs for patients with Crohn's disease in the United States. *Am J Gastroenterol* 2016;111:15–23.
4. Condino AA, Fidanza S, Hoffenberg EJ. A home infliximab infusion program. *J Pediatr Gastroenterol Nutr* 2005;40:67–9.
5. <https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/PhysicianFeeSched/Downloads/Website-POS-database.pdf>. Accessed April 4, 2017.
6. Cheifetz A, Smedley M, Martin S, et al. The incidence and management of infusion reactions to infliximab: a large center experience. *Am J Gastroenterol* 2003;98:1315–24.
7. Colombel JF, Sandborn WJ, Reinisch W, et al., SONIC Study Group. Infliximab, azathioprine, or combination therapy for Crohn's disease *N Engl J Med* 2010;362:1383–95.
8. Hutsell SQ, Wu M, Park KT. Frequency of severe infusion reactions associated with outpatient infusion of infliximab without premedications. *J Pediatr Gastroenterol Nutr* 2017;65:430–1.
9. O'Meara S, Nanda KS, Moss AC. Antibodies to infliximab and risk of infusion reactions in patients with inflammatory bowel disease: a systematic review and meta-analysis. *Inflamm Bowel Dis* 2014;20:1–6.
10. Kelsen JR, Grossman AB, Pauly-Hubbard H, et al. Infliximab therapy in pediatric patients 7 years of age and younger. *J Pediatr Gastroenterol Nutr* 2014;59:758–62.
11. Feuerstein JD, Nguyen GC, Kupfer SS, et al., American Gastroenterological Association Institute Clinical Guidelines Committee. American Gastroenterological Association Institute Guideline on therapeutic drug monitoring in inflammatory bowel disease. *Gastroenterology* 2017;153:827–34.
12. [www.nhia.org/about/ethics/standards.cfm](http://www.nhia.org/about/ethics/standards.cfm). Accessed October 1, 2017.
13. Picoraro J, Winberry G, Siegel CA, et al. Premedication use before infliximab administration: a cross-sectional analysis. *Inflamm Bowel Dis* 2017;23:174–80.
14. Kappelman MD, Bousvaros A, Hyams J, et al. Intercenter variation in initial management of children with Crohn's disease. *Inflamm Bowel Dis* 2007;13:890–5.
15. Peyrin-Biroulet L, Sandborn W, Sands BE, et al. Selecting Therapeutic Targets in Inflammatory Bowel Disease (STRIDE): determining therapeutic goals for treat-to-target. *Am J Gastroenterol* 2015;110:1324–38.
16. Park KT, Crandall WV, Fridge J, et al. Implementable strategies and exploratory considerations to reduce costs associated with anti-TNF therapy in inflammatory bowel disease. *Inflamm Bowel Dis* 2014;20: 946–51.
17. Rutgeerts P, Feagan BG, Lichtenstein GR, et al. Comparison of scheduled and episodic treatment strategies of infliximab in Crohn's disease. *Gastroenterology* 2004;126:402–13.
18. Hanauer SB, Wagner CL, Bala M, et al. Incidence and importance of antibody responses to infliximab after maintenance or episodic treatment in Crohn's disease. *Clin Gastroenterol Hepatol* 2004;2: 542–53.
19. Buisson A, Seigne AL, D'huart MC, et al. The extra burden of infliximab infusions in inflammatory bowel disease. *Inflamm Bowel Dis* 2013;19:2464–7.
20. Mackner LM, Bickmeier RM, Crandall WV. Academic achievement, attendance, and school-related quality of life in pediatric inflammatory bowel disease. *J Dev Behav Pediatr* 2012;33:106–11.
21. Buisson A, Seigne AL, D'huart MC, et al. The extra burden of infliximab infusions in inflammatory bowel disease. *Inflamm Bowel Dis* 2013;19:2464–7.
22. Kuin S, Stolte SB, van den Brink GR, et al. Short article: Remicade infusions at home: an alternative setting of infliximab therapy for patients with Crohn's disease. *Eur J Gastroenterol Hepatol* 2016; 28:222–5.
23. Petroff BJ, Filibeck D, Nowobilski-Vasilios A, et al. ASHP guidelines on home infusion pharmacy services. *Am J Health Syst Pharm* 2014;71:325–41.
24. Nuti F, Civitelli F, Bloise S, et al. Prospective evaluation of the achievement of mucosal healing with anti-TNF- $\alpha$  therapy in a paediatric Crohn's disease cohort. *J Crohns Colitis* 2016;10:5–12.
25. Rummel FM, Veres G, Kolho KL, et al. Consensus guidelines of ECCO/ESPGHAN on the medical management of pediatric Crohn's disease. *J Crohns Colitis* 2014;8:1179–207.
26. Rufo PA, Denson LA, Sylvester FA, et al. Health supervision in the management of children and adolescents with IBD: NASPGHAN recommendations. *J Pediatr Gastroenterol Nutr* 2012;55:93–108.
27. Heida A, Park KT, van Rheenen P. Clinical utility of fecal calprotectin monitoring in asymptomatic patients with inflammatory bowel disease: a systematic review and practical guide. *Inflamm Bowel Dis (in press)* 2017 Jun;23(6):894–902.
28. Geary A, Rummel APB. Improving Performance: How to Manage the White Space on the Organization Chart. 3rd ed. San Francisco, CA: Jossey-Bass; 2012.