November 5, 2024

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Dear Dr. Hashmi, Dr. Chassay, Dr. Robinson, Dr. Hoffman, Dr. Shankar, and Dr. Lechner:

On behalf of the American Society of Gastrointestinal Endoscopy (ASGE), the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN), the American College of Gastroenterology (ACG), and the American Gastroenterological Association (AGA), we write regarding Blue Cross Blue Shield's (BCBS) draft policy on "Infliximab and Associated Biosimilars," Policy Number: RX501.051 with an effective date of Jan. 1, 2025.

The only drugs under the impending policy with preferred status are Avsola and Inflectra. Finalizing this policy will unquestionably have a detrimental impact on timely patient access to care and will lead to higher out-of-pocket costs for BCBS beneficiaries who rely on biologic products to treat their inflammatory bowel disease (IBD) — Crohn's Disease and ulcerative colitis. **We collectively urge BCBS to amend its draft policy to include Remicade as a preferred drug for the conditions listed in the policy.** Further, we ask BCBS to expressly state in the policy that patients currently on Remicade

will be able to continue with Remicade, without being subjected to prior authorization, step therapy protocols, or other cost-management utilization requirements.

Our organizations also object to coverage exclusions of concurrent use of infliximab and infliximab biosimilars with other biologics. We are also concerned with the ability of BCBS's pediatric patients to access higher dosing levels when recommended by the treating physician.

FORMULARY EXCLUSIONS

Our organizations support the use of biosimilars for the management of IBD. However, their use in the physician office setting has been limited by reimbursement rates that typically fall well below physician acquisition costs. For example, a physician practice's typical acquisition cost for a unit of Inflectra ranges $300-$400, far exceeding average sales prices, the basis for reimbursement:

Inflectra 100 mg
Q1 2024: $142.94
Q2 2024: $110.92
Q3 2024: $106.63

Avsola 100 mg
Q1 2024: $142.94
Q2 2024: $110.92
Q3 2024: $106.63

Gastroenterology practices have begun sending patients on Inflectra or Avsola to the hospital outpatient setting for their infusions. When physician practices must shift a patient to the hospital setting, the result is higher out-of-pocket costs to the patient and to the health care system. As more physician practices shift their patients to hospitals for their infusions, timely access to care will be compromised because hospitals do not have infinite capacity. When patients must move to another site of care for their infusions, care is often delayed because patients need to determine which infusion centers are in-network and able to provide one of the two preferred infliximab products; obtain an appointment; and wait for prior authorization. These processes take time that patients in active treatment or in need of treatment cannot spare. When IBD patients experience delays in care, the result can be loss of treatment response, malnutrition, hospitalization, surgery, and even death.

We appreciate the draft policy would allow continuation of therapy with non-preferred drugs when considered medically necessary, as determined by our members, including new BCBS enrollees. Treating physicians, however, will need to again prove medical necessity siphoning resources away from direct patient care. Unfortunately, patients who are approved for a non-preferred drug will have higher out-of-pocket costs. When patients can't afford higher costs for non-preferred drugs, their only choice may be to switch to a preferred drug even though they may be stable or experiencing disease improvement on their current therapy.

Preferred drug utilization management tools infringe on the patient-physician relationship and more often than not, inhibit access to prescribed care. The physician is in the best position to decide the best

course of treatment for their patients and your beneficiaries. Formulary changes that result in non-medical switching are occurring with increasing frequency at the expense of IBD patients.

IBD patients are vulnerable to potential immunogenicity from multiple non-medical therapy switches throughout their lifetimes caused by preferred drug utilization management. Many patients have already been subjected to medication changes for non-medical reasons. This risk in pediatric patients is clearly established in well-documented, large epidemiologic studies that show children with IBD have more severe disease phenotype than adult-onset IBD[1] which further impacts how the pediatric patient will respond to biologic agents. Children have the unfortunate unique situation with a longer lifetime burden of disease, including increased risk for progression to certain types of intestinal cancer if inflammation is not kept under appropriate control. Without restrictions of non-medical switching, children and adults are at risk of being repeatedly forced to switch on and off biologic therapies. Anecdotally, we all have cases where our patients have been forced to switch biosimilars multiple times and sometimes back to the originator biologic with the result being complete loss of efficacy or serious adverse reactions.

PEDIATRIC DOSING

Childhood IBD is more aggressive than adult disease, causing more disease-related complications.[2,3] This is further complicated by children commonly having rapid clearance of biologic medications compared to adults.[4-6] The original dosing of infliximab and adalimumab, first recommended by the U.S. Food and Drug Administration (FDA) more than 25 years ago, have been repeatedly found to be ineffective for children with IBD.[4-8] Limiting dosing based on outdated and obsolete recommendations results in under-treatment, is contrary to current standards of care, and is associated with worsening disease, which increases the need for hospitalization and surgical intervention.[9-10] Infliximab and adalimumab dosing should be guided by disease severity, and by therapeutic drug monitoring.[12,13] This is supported by numerous professional society guidelines and is considered standard of care.[14-17] For example, the ACG consensus statement recommends adjusting infliximab dosing to achieve infliximab trough levels of 10-15 mcg/ml for patients with inadequate response at lower levels.[17] Those with aggressive disease may require even higher serum trough levels >20 mcg/ml maintain remission.[6,18,19] A policy limiting a child's biologic therapy to known sub-therapeutic dosing is a deviation from standard of care, is highly likely to cause harm, is unethical, and should not be endorsed by this draft policy or any policy.[11-14] Further, delays in initiating appropriate dosing causes harm, particularly to children with IBD.[9,20-21]

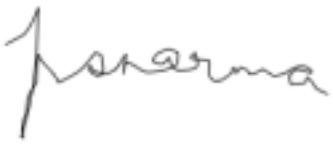
We ask that BCBS use the most current literature to guide review of requests for higher dosing.

DUAL BIOLOGIC THERAPY

Dual biologic and and other advanced combination therapies (ACT) are not commonly used in treating patients with IBD. However, for children with the most aggressive disease, ACT is necessary.[23,24] There is growing evidence of the efficacy and safety of ACT in treating patients with IBD unresponsive to multiple single biologic medications.[25-27] A policy which explicitly and unambiguously forbids use of infliximab or adalimumab concurrently with other biologics will deny care to the most vulnerable patients with the most aggressive disease. **We urge BCBS to revise its policy to permit dual biologic therapy in medically necessary situations.**

Our societies welcome a virtual meeting opportunity to expand upon these concerns and answer questions you may have. Additionally, we request that the comment period on the draft policy be reopened to provide ample opportunity for physicians in affected states to respond. To arrange a meeting, please contact Camille Bonta, ASGE and NASPGHAN, at cbonta@summithealthconsulting.com; Brad Conway, ACG, at bconway@gi.org; and Kathleen Teixeira, AGA, at kteixeira@gastro.org.

Sincerely,



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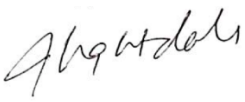

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