June 9, 2021

Young Fried, PharmD, MSP
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Dear Dr. Fried,

Thank you for meeting with us on May 24 to discuss Cigna's Drug and Biologic Coverage Policy M0003. We truly appreciate your team's time and willingness to help us better understand the policy change and engage in an open discussion about issues of concern to our members. Below please find our recommendations for consideration as you prepare for implementation of the policy changes.

Notification

- Increase the number of notifications sent to physicians about this policy change including letters, email and social media
    - Include in the notices that Cigna is now accepting prior authorization (PA) requests to keep patients who should not switch on Remicade and encourage physicians to submit PA requests as soon as possible
- Include additional information on the safety of switching to biosimilars in all patient communications

We appreciate the efforts Cigna has made to educate patients and physicians about Cigna's new policy to switch patients from Remicade to Inflectra or Avsola beginning July 1; however, based on feedback from our members, many physicians have not received the new policy, and they are learning about the change from their patients. **We urge Cigna to increase its outreach efforts to physicians, including more written notices and email outreach than what has already been planned.** We also request that requests for PA be completed in a timely manner with genuine peer review.

We thank Cigna for including patient identification information for those currently on Remicade in its letters to physicians to help them identify patients impacted by the policy change. **In addition to this information, we urge Cigna to include in all future physician communications that PA requests to keep patients on Remicade are being accepted now and encourage physicians to submit PA requests as soon as possible so there is no disruption of biological therapy for the patient.**

On our call, Dr. Sundeep Singh stressed the importance of Cigna providing more information on the safety of switching in its communications to impacted patients. Dr. Edwin de Zoeten offered that it is particularly difficult to have conversations with pediatric patients' families because there is very little to no data on the safety of switching in pediatric patients, the longevity of maintenance or the immunogenicity, which presents an even greater challenge. While we agree that ideally patients and physicians should have this discussion together, there isn't enough time to schedule patient appointments before Cigna's policy takes effect in approximately one month. **We understand that Cigna is not considering an implementation delay for the policy change; therefore, we urge Cigna to help physicians by providing basic information on the safety of biosimilars in its patient communications.**

Exceptions

- Create an exception to allow the following highly vulnerable populations to remain on Remicade:
    - Children 16 years of age and younger
    - Pregnant women
    - Children older than 16 years of age and adults currently having an active flare of disease
    - Patients of any age currently in the induction period for Remicade at the time the policy change takes effect
- Reduce administrative burden by not requiring physicians to submit PA to keep patients falling under an exception on Remicade
- Aggressively promote any new exceptions to both physicians and patients so all parties are aware prior to July 1

We strongly recommend creating an exception that allows children and pregnant women to remain on Remicade. The lack of abundant clinical literature on the effects of non-medical switching in these populations should not be interpreted as an indication that it can or should be done. As Dr. Edwin de Zoeten said in our discussion, "Children are not little adults." Specifically, **we recommend allowing children 16 years of age and younger be allowed to stay on their current drug.** Dr. Gilaad Kaplan's study, *The Argument Against a Biosimilar Switch Policy for Infliximab in Patients with Inflammatory Bowel Disease Living in Alberta*[1], concluded "Nonmedical switching has not been adequately studied in highly vulnerable populations including children, pregnant women and elderly patients." In addition, the young, specifically, have a greater issue with immunogenicity.[2] Switching puts them at greater risk of loss of an effective drug due to development of antibodies and switching to a biosimilar exposes them without reason to the risk of antibody development. This question of immunogenicity in children has not been addressed in biosimilar studies and, therefore, there is not data to suggest safety.

[1] Kaplan GG, Ma C, Seow CH, Kroeker KI, Panaccione R. The Argument Against a Biosimilar Switch Policy for Infliximab in Patients with Inflammatory Bowel Disease Living in Alberta. J Can Assoc Gastroenterol. 2020;3(5):234-242. doi:10.1093/jcag/gwz044

[2] Kelsen JR, Grossman AB, Pauly-Hubbard H, Gupta K, Baldassano RN, Mamula P. Infliximab therapy in pediatric patients 7 years of age and younger. J Pediatr Gastroenterol Nutr. 2014 Dec;59(6):758-62. doi: 10.1097/MPG.0000000000000533. PMID: 25419596.

Patients currently undergoing an active flare of disease should not be required to switch. Switching could result in increased hospitalizations and surgeries which would increase costs to Cigna. We were unable to locate studies involving switching involving patients undergoing an active flare. We believe patients undergoing an active flare would be excluded from any study for ethical reasons.

Patients who began Remicade before the policy change should be allowed to continue for their first 12 months before being required to switch. The paper *Process and Clinical Outcomes of a Biosimilar Adoption Program with Infliximab-Dyyb*[3] is a retrospective cohort study that supports our requested exceptions for adult patients. In March 2018, Boston Medical Center decided to adopt infliximab-dyyb and transition patients who had been on infliximab for ≥ 6 months for all indications to infliximab -dyyb. According to the findings of the study, 38% of patients required dose increase within a year while the infliximab group rarely required dose escalation.

If Cigna creates exceptions to its policy, it is vital that both physicians and patients are made aware and the process for exceptions not be administratively burdensome. Our experience with other insurers that have created exceptions for certain patient populations is that when extensive outreach was not done to education physicians and patients, some patients meeting the exception criteria were switched. Not only are we aware of adverse outcomes that resulted in some patients, but pediatric patients who should not be switched multiple times and should not go back to the originator biologic after a switch are now at a therapeutic disadvantage in the future. The process of switching also causes undue stress to patients and their families.

Out of pocket costs

- Increase patient awareness of the potential for increases in out of pocket costs that may result from this policy change

We urge Cigna to provide clear information to its patients regarding the potential impact of out of pocket costs that could result from this policy change. This responsibility and administrative burden should not fall on the shoulders of physicians who are often the first line of contact when patients must absorb an unexpected cost. Physician office staff are frequently saddled with the burden of explaining the how the insurer's policy change resulted in the increase cost to the patient.

Reducing administrative burden

- Communicate to physicians the process for the following situations:
    - Switching a patient to Inflectra or Avsola without a change in dosing or site or service
    - Switching a patient to Inflectra or Avsola that requires a change to dosing or site of service
    - Requesting PA to keep a patient on Remicade
    - Appealing a denial and requesting peer-to-peer review

[3] Bhat S, Altajar S, Shankar D, Zahorian T, Robert R, Qazi T, Shah B, Farraye FA. Process and Clinical Outcomes of a Biosimilar Adoption Program with Infliximab-Dyyb. J Manag Care Spec Pharm. 2020 Apr;26(4):410-416. doi: 10.18553/jmcp.2020.26.4.410. PMID: 32223602.

We applaud Cigna for actively working to reduce administrative burden to physicians for patients who can be switched from Remicade to Inflecta and Avsola without changes to dosing or site of service. However, more must be done to communicate this information clearly and quickly to physicians. Physicians and their staff need clear directions on Cigna's processes for switching patients who require dosing or site or service changes, requesting PA to keep a patient on Remicade, appealing a denial and requesting peer-to-peer review. **We strongly urge Cigna to provide this information to physicians and their staff via additional outreach through mail, email and social media.**

Supporting literature

We would also like to share the following additional supporting literature.

Dipasquale V, Romano C. Biosimilar infliximab in paediatric inflammatory bowel disease: Efficacy, immunogenicity and safety. Clin Pharm Ther. 2020;45:1228–1234. doi: 10.1111/jcpt.13239

Kaplan GG, Ma C, Seow CH, Kroeker KI, Panaccione R. The Argument Against a Biosimilar Switch Policy for Infliximab in Patients with Inflammatory Bowel Disease Living in Alberta. J Can Assoc Gastroenterol. 2020;3(5):234-242. doi:10.1093/jcag/gwz044

Fitzgerald T, Melsheimer R, Lafeuille MH, Lefebvre P, Morrison L, Woodruff K, Lin I, Emond B. Switching and Discontinuation Patterns Among Patients Stable on Originator Infliximab Who Switched to an Infliximab Biosimilar or Remained on Originator Infliximab. Biologics. 2021;15:1-15 https://doi.org/10.2147/BTT.S285610

Gecse KB, Lovász BD, Farkas K, Banai J, Bene L, Gasztonyi B, Golovics PA, Kristóf T, Lakatos L, Csontos ÁA, Juhász M, Nagy F, Palatka K, Papp M, Patai Á, Lakner L, Salamon Á, Szamosi T, Szepes Z, Tóth GT, Vincze Á, Szalay B, Molnár T, Lakatos PL. Efficacy and Safety of the Biosimilar Infliximab CT-P13 Treatment in Inflammatory Bowel Diseases: A Prospective, Multicentre, Nationwide Cohort. J Crohns Colitis. 2016 Feb;10(2):133-40. doi: 10.1093/ecco-jcc/jjv220. Epub 2015 Dec 10. PMID: 26661272.

[2]Kelsen JR, Grossman AB, Pauly-Hubbard H, Gupta K, Baldassano RN, Mamula P. Infliximab therapy in pediatric patients 7 years of age and younger. J Pediatr Gastroenterol Nutr. 2014 Dec;59(6):758-62. doi: 10.1097/MPG.0000000000000533. PMID: 25419596.

We thank you again for taking time to speak with us. If you have any questions, please contact Leslie Narramore, AGA, at 410-349-7455 or Lnarramore@gastro.org; Lakitia Mayo, ASGE, at 630-570-5641 or lmayo@asge.org; Camille Bonta, NASPGHAN, at 202-320-3658 or cbonta@summithealthconsulting.com and Brad Conway, ACG, at 301-263-9000 or bconway@gi.org;

Sincerely,

American College of Gastroenterology
American Gastroenterological Association
American Society for Gastrointestinal Endoscopy
North American Society for Pediatric Gastroenterology, Hepatology and Nutrition